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 ********** STN Columbus *******
**********
FILE 'MEDLINE'
FILE 'JAPIO'
FILE 'BIOSIS'
FILE 'SCISEARCH
FILE 'WPIDS'
FILE 'CAPLUS'
FILE 'EMBASE'
=> s calcium channel#

L1     141663 CALCIUM CHANNEL#

=> s l1 and (t-type or t type)

  5 FILES SEARCHED...
L2       3515 L1 AND (T-TYPE OR T TYPE)

=> s l2 and (alpha-1 or alpha 1 or alpha1)

  5 FILES SEARCHED...
  6 FILES SEARCHED...
L3       216 L2 AND (ALPHA-1 OR ALPHA 1 OR
ALPHA1)

=> s l3 and (agonist# or antagonist#)

L4       51 L3 AND (AGONIST# OR
ANTAGONIST#)

=> dup rem l4

PROCESSING COMPLETED FOR L4
L5       21 DUP REM L4 (30 DUPLICATES
REMOVED)

=> dup rem l3

PROCESSING COMPLETED FOR L3
L6       104 DUP REM L3 (112 DUPLICATES
REMOVED)

=> d l5 cit ibib abs 1-21

=> d l5 ibib abs 1-21


L5  ANSWER 1 OF 21  WPIDS COPYRIGHT 2001
DERWENT INFORMATION LTD
ACCESSION NUMBER:    2000-271475 [23]
WPIDS
DOC. NO. CPI:        C2000-082967
TITLE:               Novel nucleic acids encoding
pancreatic  ***T*** -
                     ***type***  ***calcium***
***channels***  used
                     for regulation of  ***T*** -
***type***
                     ***calcium***  ***channels***  and
treatment of type
                     II diabetes.
DERWENT CLASS:       B04 D16
INVENTOR(S):         LI, M
PATENT ASSIGNEE(S):  (SALA-N) SOUTH
ALABAMA MEDICAL SCI FOUND
COUNTRY COUNT:       83
PATENT INFORMATION:

   PATENT NO  KIND DATE    WEEK    LA  PG
   ---------------------------------------
   WO 2000015845 A1 20000323 (200023)* EN  124
     RW: AT BE CH CY DE DK EA ES FI FR GB
GH GM GR IE IT KE LS LU MC MW NL
         OA PT SD SE SL SZ UG ZW
      W: AL AM AT AU AZ BA BB BG BR BY CA
CH CN CU CZ DE DK EE ES FI GB GD
         GE GH GM HR HU ID IL IN IS JP KE KG KP
KR KZ LC LK LR LS LT LU LV
         MD MG MK MN MW MX NO NZ PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT
         UA UG UZ VN YU ZW
   AU 9960217   A  20000403 (200034)

APPLICATION DETAILS:

   PATENT NO  KIND          APPLICATION
DATE
   ---------------------------------------
   WO 2000015845 A1          WO 1999-US19675
19990826
   AU 9960217   A            AU 1999-60217
19990826

FILING DETAILS:

   PATENT NO  KIND          PATENT NO
   ---------------------------------------
   AU 9960217   A  Based on  WO 200015845

PRIORITY APPLN. INFO: US 1999-117399
19990127; US 1998-98004
                19980826
AN  2000-271475 [23]  WPIDS
AB  WO 200015845 A UPAB: 20000516
   NOVELTY - An isolated pancreatic  ***T*** -
***type***
    ***calcium***  ***channel***  (I) is new.
      DETAILED DESCRIPTION - INDEPENDENT
CLAIMS are also included for the
   following:
      (1) an isolated nucleic acid molecule (NAM) (II)
encoding (I);
      (2) an antisense NAM (III) complementary to
(II);
      (3) a cell comprising (III);
      (4) an expression vector comprising (III);
      (5) a method (A) of decreasing expression of a (I)
in a host cell;
      (6) a ribozyme (IV) having a recognition
sequence complementary to a
   portion of (II);
      (7) a cell comprising (IV);
      (8) an expression vector comprising (IV);
      (9) a cell comprising (II);
      (10) an expression vector comprising (II);
      (11) a method (B) of increasing expression of (II)
in a host cell,
   comprising introducing (I) into the cell;
      (12) a method (C) of screening a substance for
the ability to modify
   the function of (I);
      (13) a method (D) of obtaining DNA encoding
(II)
      (14) a DNA oligomer capable of hybridizing to
(I);
      (15) a method (E) of detecting presence of a
pancreatic  ***T*** -
    ***type***  ***calcium***  ***channel***
in a sample,
      (16) an antibody (V) specific for (II); and
      (17) a method of detecting the presence of (I) in a
sample,
   comprising contacting the sample with (V) and
detecting the complex
   formed.
      ACTIVITY - antidiabetic.
      MECHANISM OF ACTION - The polypeptide
functions as a pancreatic
    ***T*** -  ***type***  ***calcium***
***channel*** .
      USE - The pancreatic  ***T*** -  ***type***
***calcium***
    ***channel***  polynucleotides and polypeptides
are used for treating
   diseases associated with abnormal expression or
function of  ***T*** -
    ***type***  ***calcium***  ***channels***
. They are especially
   used for treating type II diabetes (claimed). They are
used in methods for
   modifying insulin secretion by pancreatic beta cells,
for modifying basal
   calcium levels in cells, for modifying the action of
potential L type
    ***calcium***  ***channels***  in cells, for
modifying pancreatic cell
   death, for modifying pancreatic beta cell
proliferation, and for modifying
   calcium influx through L type  ***calcium***
***channels***  in
   cells (all claimed). The polypeptides are used to
produce antibodies,
   which can be used in assays to identify cells or
tissues which express
   pancreatic  ***T*** -  ***type***
***calcium***  ***channels***
   , or for detecting pancreatic  ***T*** -
***type***  ***calcium***
    ***channels***  in samples. Antisense sequences
and ribozymes can be used
   to decrease expression of pancreatic  ***T*** -
***type***
    ***calcium***  ***channels***  . Inhibitors
and  ***antagonists***
   (identified using the polypeptides of the invention)
can be used to
   decrease the activity of pancreatic  ***T*** -
***type***
    ***calcium***  ***channels***  .
      ADVANTAGE - No stated advantage given in
the specification.
      DESCRIPTION OF DRAWING(S) - The figure
is a schematic illustration
   representing the partial rat genomic nucleotide
composition between
   domains III and IV. Genomic DNA contained an
exon specific to alpha 1G
   (shaded circle) and an exon specific to the
***alpha***  ***1***
   subunit of  ***T*** -  ***type***  Ca2+
deduced from INS-1 (shaded
   rectangle). Other exons (open rectangles) are
identical between the two
   cDNAs. The bold letters indicate the nucleotide
coding Gly1667.
   Dwg.1b/25

L5  ANSWER 2 OF 21  BIOSIS  COPYRIGHT 2001
BIOSIS    DUPLICATE 1
ACCESSION NUMBER:    2000:447682 BIOSIS
DOCUMENT NUMBER:     PREV200000447682
TITLE:               Influence of  ***T*** -  ***type***
Ca2+ (mibefradil)
                     and Cl- (indanyloxyacetic acid 94) channel
                     ***antagonists***  on  ***alpha1***
-adrenoceptor
                     mediated contractions in rat aorta.
AUTHOR(S):           Duggan, Jennifer A.; Tabrizchi,
Reza (1)
CORPORATE SOURCE:    (1) Division of Basic
Medical Sciences, Faculty of
                     Medicine, Memorial University of
Newfoundland, Saint
                     John's, NF, A1B 3V6 USA
SOURCE:              Canadian Journal of Physiology and
Pharmacology,
                     (September, 2000) Vol. 78, No. 9, pp.
714-720. print.
                     ISSN: 0008-4212.
DOCUMENT TYPE:       Article
LANGUAGE:            English
SUMMARY LANGUAGE:    English; French
AB  The effects of the  ***T*** -  ***type***  and
L-type Ca2+ channel
    ***antagonists***  , mibefradil and nifedipine,
respectively, and those of
   a Cl- channel  ***antagonist***  , indanyloxyacetic
acid 94, on
   mechanical responses elicited by selective activation
of  ***alpha1***
   -adrenoceptors using cirazoline were examined in rat
isolated aortic
   rings. The presence of mibefradil (300 nM),
indanyloxyacetic acid, 94 (30
   muM) and nifedipine (300 nM) alone inhibited
mechanical responses elicited
   by cirazoline. The concentration-response curves to
cirazoline were
   displaced to the right with significant increases in the
EC50 and
   significant depressions of the maximal responses in
the presence of the
   individual agents mibefradil, indanyloxyacetic acid
94, or nifedipine. A
   combination of mibefradil and indanyloxyacetic acid
94 further inhibited
   the mechanical activity produced by cirazoline. The
further reduction in
   the maximal response to cirazoline, in the presence
of mibefradil and
   nifedipine, was insignificant when compared with
the effects of nifedipine
   alone. In addition, maximal mechanical responses
produced by cirazoline
   were not significantly affected by a combination of
nifedipine and
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indanyloxyacetic acid 94 when compared with either nifedipine alone or
mibefradil and indanyloxyacetic acid 94 combined. Our current findings
indicate that mibefradil, indanyloxyacetic acid 94, and nifedipine can
inhibit cirazoline-induced contractions to a varying degree. Moreover,
based on our present data it would be reasonable to suggest that the
contribution of ***T*** - ***type*** versus L-type Ca2+ channels to
contractile responses obtained with cirazoline are approximately 21% and
35%, respectively, of the Emax. It would appear that L-type Ca2+ channels
play a greater role in processes that are involved in excitation-
contraction coupling subsequent to stimulation of ***alpha1*** -adrenoceptors. In addition, Cl- channels also appear to be involved in
the process of contraction following ***alpha1*** -adrenoceptor
activation.

L5 ANSWER 3 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000352205 EMBASE
TITLE: Mibefradil block of cloned ***T*** - ***type***
calcium ***channels*** .
AUTHOR: Martin R.L.; Lee J.-H.; Cribbs L.L.; Perez-Reyes E.; Hanck
D.A.
CORPORATE SOURCE: Dr. D.A. Hanck, Cardiology (MC6094), University of Chicago,
5841 South Maryland Ave., Chicago, IL 60637, United States.
d-hanck@uchicago.edu
SOURCE: Journal of Pharmacology and Experimental Therapeutics,
(2000) 295/1 (302-308).
Refs: 34
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mibefradil is a tetralol derivative chemically distinct from other
calcium ***channel*** ***antagonists*** . It is a very
effective antihypertensive agent that is thought to achieve its action via
a higher affinity block for low-voltage-activated (T) than for
high-voltage-activated (L) ***calcium*** ***channels*** . Estimates
of affinity using Ba2+ as the charge carrier have predicted a 10- to
15-fold preference of mibefradil for T channels over L channels. However,
T channel IC50 values are reported to be .apprx.1 .mu.M, which is much
higher than expected for clinical efficacy because relevant blood levels
of this drug are .apprx.50 nM. We compared the affinity for mibefradil of
the newly cloned T channel isoforms, .alpha.1G, .alpha.1H, and .alpha.1I
with an L channel, .alpha.1C. In 10 mM Ba2+, mibefradil blocked in the
micromolar range and with 12- to 13-fold greater affinity for T channels
than for L channels (.apprx.1 .mu.M versus 13/.mu.M). When 2 mM Ca2+ was
used as the charge carrier, the drug was more efficacious; the IC50 for
.alpha.1G shifted to 270 nM and for . ***alpha*** . ***1*** H shifted
to 140 nM, 4.5- and 9-fold higher affinity than in 10 mM Ba. The data are
consistent with the idea that mibefradil competes for its binding site on
the channel with the permeant species and that Ba2+ is a more effective
competitor than Ca2+. Raising temperature to 35.degree.C reduced affinity
(IC50 792 nM). Reducing channel availability to half increased affinity
(.apprx.70 nM). This profile of mibefradil affinity makes these channels
good candidates for the physiological target of this antihypertensive
agent.

L5 ANSWER 4 OF 21 MEDLINE
DUPLICATE 2
ACCESSION NUMBER: 2000127580 MEDLINE
DOCUMENT NUMBER: 20127580
TITLE: Determinants of voltage-dependent inactivation affect
Mibefradil block of ***calcium*** ***channels*** .
AUTHOR: Jimenez C; Bourinet E; Leuranguer V; Richard S; Snutch T P;
Nargeot J
CORPORATE SOURCE: Institut de Genetique Humaine, CNRS UPR1142, Montpellier,
France.
SOURCE: NEUROPHARMACOLOGY, (2000) 39 (1) 1-10.
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000404
AB The voltage gated ***calcium*** ***channel*** family is a major
target for a range of therapeutic drugs. Mibefradil (Ro 40-5967) belongs
to a new chemical class of these molecules which differs from other Ca2+
antagonists by its ability to potently block ***T*** -
type Ca2+ channels. However, this molecule has also been shown to
inhibit other Ca2+ channel subtypes. To further analyze the mechanism
governing the Ca2+ channel-Mibefradil interaction, we examined the effect
of Mibefradil on various recombinant Ca2+ channels expressed in mammalian
cells from their cloned cDNAs, using Ca2+ as the permeant ion at
physiological concentration. Expression of alpha1A, alpha1C, and alpha1E
in tsA 201 cells resulted in Ca2+ currents with functional characteristics
closely related to those of their native counterparts. Mibefradil blocked
alpha1A and alpha1E with a Kd comparable to that reported for ***T*** -
type channels, but had a lower affinity (approximately 30-fold)
for alpha1C. For each channel, inhibition by Mibefradil was consistent
with high-affinity binding to the inactivated state. Modulation of the
voltage-dependent inactivation properties by the nature of the coexpressed
beta subunit or the ***alpha1*** splice variant altered block at the
Mibefradil receptor site. Therefore, we conclude that the tissue and
sub-cellular localization of ***calcium*** ***channel*** subunits
as well as their specific associations are essential parameters to
understand the in vivo effects of Mibefradil.

L5 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:377851 CAPLUS
DOCUMENT NUMBER: 131:29119
TITLE: Low-voltage activated ***calcium***
channel proteins and cDNAs encoding them and
the development of ***calcium*** ***channel***
blockers
INVENTOR(S): Williams, Mark; Stauderman, Kenneth; Harpold, Michael;
Hans, Michael; Urrutia, Arturo; Washburn, Mark S.
PATENT ASSIGNEE(S): Sibia Neurosciences, Inc., USA
SOURCE: PCT Int. Appl., 171 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9928342	A2	19990610	WO 1998-US25671	19981203
WO 9928342	A3	19990826		

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
AU 9918026 A1 19990616 AU 1999-18026 19981203
EP 1042468 A2 20001011 EP 1998-962884 19981203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: US 1997-984709 19971203
US 1998-188932 19981110
WO 1998-US25671 19981203

AB CDNAs for alternative splicing forms of the . ***alpha*** . ***1*** subunit of the ***T*** - ***type*** or low-voltage activated ***calcium*** ***channel*** are cloned and characterized. The cDNAs
may be used in the development of systems for screening for effectors of
the ***calcium*** ***channel*** for therapeutic use. Candidate
clones were first generated by PCR using degenerate primers targeted
against sequences encoding conserved regions of the protein. A series of
overlapping cDNAs encoding two .alpha.1H subtypes were obtained and
full-length cDNAs constructed. The electrophysiol. and pharmacol. of the
channels was studied in Xenopus oocytes.

L5 ANSWER 6 OF 21 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 1999127945 MEDLINE
DOCUMENT NUMBER: 99127945
TITLE: Structure and functional characterization of a novel human
low-voltage activated ***calcium*** ***channel*** .
AUTHOR: Williams M E; Washburn M S; Hans M; Urrutia A; Brust P F;
Prodanovich P; Harpold M M; Stauderman K A
CORPORATE SOURCE: SIBIA Neurosciences Inc., La Jolla, California 92037, USA.
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1999 Feb) 72 (2) 791-9.
Journal code: JAV. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF073931

ENTRY MONTH: 199904
AB We have isolated and characterized overlapping cDNAs encoding a novel,
voltage-gated Ca2+ channel ***alpha1*** subunit, alpha1H, from a human
medullary thyroid carcinoma cell line. The alpha1H subunit is structurally
similar to previously described ***alpha1*** subunits. Northern blot
analysis indicates that alpha1H mRNA is expressed throughout the brain,
primarily in the amygdala, caudate nucleus, and putamen, as well as in
several nonneuronal tissues, with relatively high levels in the liver,
kidney, and heart. Ba2+ currents recorded from human embryonic kidney 293
cells transiently expressing alpha1H activated at relatively
hyperpolarized potentials (-50 mV), rapidly inactivated (tau = 17 ms), and
slowly deactivated. Similar results were observed in Xenopus oocytes
expressing alpha1H. Single-channel measurements in human embryonic kidney
293 cells revealed a single-channel conductance of approximately 9 pS.
These channels are blocked by Ni2+ (IC50 = 6.6 microM) and the ***T***
- ***type*** channel ***antagonists*** mibefradil (approximately
50% block at 1 microM) and amiloride (IC50 = 167 microM). Thus,
alpha1H-containing channels exhibit biophysical and pharmacological
properties characteristic of low voltage-activated, or ***T*** -
type , Ca2+ channels.

L5 ANSWER 7 OF 21 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
ACCESSION NUMBER: 2000:85729 BIOSIS
DOCUMENT NUMBER: PREV200000085729
TITLE: Determinants of voltage-dependent inactivation affect
Mibefradil block of ***calcium*** ***channels*** .
AUTHOR(S): Jimenez, Cristina; Bourinet, Emmanuel; Leuranguer, Valerie;
Richard, Sylvain; Snutch, Terry P.; Nargeot, Joel (1)
CORPORATE SOURCE: (1) Institut de Genetique Humaine, CNRS UPR1142, 141 Rue de
la Cardonille, 34396, Montpellier Cedex 5 France
SOURCE: Neuropharmacology, (Dec. 17, 1999) Vol. 39, No. 1, pp.
1-10.
ISSN: 0028-3908.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The voltage gated ***calcium*** ***channel*** family is a major
target for a range of therapeutic drugs. Mibefradil (Ro 40-5967) belongs
to a new chemical class of these molecules which differs from other Ca2+
antagonists by its ability to potently block ***T*** -
type Ca2+ channels. However, this molecule has also been shown to
inhibit other Ca2+ channel subtypes. To further analyze the mechanism
governing the Ca2+ channel-Mibefradil interaction, we examined the effect
of Mibefradil on various recombinant Ca2+ channels expressed in mammalian
cells from their cloned cDNAs, using Ca2+ as the permeant ion at
physiological concentration. Expression of alpha1A, alpha1C and alpha1E in
tsA 201 cells resulted in Ca2+ currents with functional characteristics
closely related to those of their native counterparts. Mibefradil blocked
alpha1A and alpha1E with a Kd comparable to that reported for ***T*** -
type channels, but had a lower affinity (apprx30-fold) for
alpha1C. For each channel, inhibition by Mibefradil was consistent with
high-affinity binding to the inactivated state. Modulation of the
voltage-dependent inactivation properties by the nature of the coexpressed
beta subunit or the ***alpha1*** splice variant altered block at the
Mibefradil receptor site. Therefore, we conclude that the tissue and
sub-cellular localization of ***calcium*** ***channel*** subunits
as well as their specific associations are essential parameters to
understand the in vivo effects of Mibefradil.

L5 ANSWER 8 OF 21 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:866265 SCISEARCH
THE GENUINE ARTICLE: 136YV
TITLE: Selective peptide ***antagonist*** of the class E
calcium ***channel*** from the venom of the
tarantula Hysterocrates gigas
AUTHOR: Newcomb R (Reprint); Szoke B; Palma A; Wang G; Chen X H;
Hopkins W; Cong R; Miller J; Urge L; TarczyHornoch K; Loo
J A; Dooley D J; Nadasdi L; Tsien R W; Lemos J; Miljanich
G
CORPORATE SOURCE: ELAN PHARMACEUT INC, 3760 HAVEN AVE, MENLO PK, CA 94025
(Reprint); UNIV MASSACHUSETTS, MED CTR, DEPT PHYSIOL,
WORCESTER, MA 01655; WARNER LAMBERT PARKE DAVIS, PARKE
DAVIS PHARMACEUT RES DIV, DEPT CHEM, ANN ARBOR, MI 48105;
WARNER LAMBERT PARKE DAVIS, PARKE DAVIS PHARMACEUT RES
DIV, DEPT NEUROSCI THERAPEUT, ANN ARBOR, MI 48105;
STANFORD UNIV, BECKMAN CTR, DEPT MOL & CELLULAR PHYSIOL,
STANFORD, CA 94305
COUNTRY OF AUTHOR: USA
SOURCE:. BIOCHEMISTRY, (3 NOV 1998) Vol. 37, No. 44, pp.
15353-15362.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,
WASHINGTON, DC 20036.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 75
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We describe the first potent and selective blocker of the class E
Ca2+-channel. SNX-482, a novel 41 amino acid peptide present in the venom
of the African tarantula, Hysterocrates gigas, was identified through its
ability to inhibit human class E Ca2+ channels stably expressed in a
mammalian cell line. An IC50 of 15-30 nM was obtained for block of the
class E Ca2+ channel, using either patch clamp electrophysiology or
K+-evoked Ca2+ flux. At low nanomolar concentrations, SNX-482 also blocked
a native resistant or R-type Ca2+ current in rat neurohypophyseal nerve
terminals, but concentrations of 200-500 nM had no effect on R-type Ca2+
cut-rents in several types of rat central neurons. The peptide has the
sequence GVDKAGCRYMFGGCSVNDDCCPRLGCHSLFSY CAWDLTFSD-OH and is homologous to
the spider peptides grammatoxin S1A and hanatoxin, both peptides with very
different ion channel blocking selectivities. No effect of SNX-482 was
observed on the following ion channel activities: Na+ or K+ currents in
several cultured cell types (up to 500 nM); K+ current through cloned
potassium channels Kv1.1 and Kv1.4 expressed in Xenopus oocytes (up to 140
nM); Ca2+ flux through L- and ***T*** - ***type*** Ca2+ channels in
an anterior pituitary cell line (GH3, up to 500 nM); and Ba2+ current
through class A Ca2+ channels expressed in Xenopus oocytes (up to 280 nM).
A weal; effect was noted on Ca2+ current through cloned and stably
expressed class B Ca2+ channels (IC50 > 500 nM). The unique selectivity of
SNX-482 suggests its usefulness in studying the diversity, function, and
pharmacology of class E and/or R-type Ca2+ channels.

L5 ANSWER 9 OF 21 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1998420198 MEDLINE
DOCUMENT NUMBER: 98420198
TITLE: Mechanisms of spontaneous cytosolic Ca2+ transients in
differentiated human neuronal cells.
AUTHOR: Gao Z Y; Chen M; Collins H W; Matschinsky F M; Lee V M;
Wolf B A
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University
of Pennsylvania School of Medicine, Philadelphia 19104,
USA.
CONTRACT NUMBER: AG09215 (NIA)
AG11542 (NIA)
AG10124 (NIA)
+
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (1998 Jul) 10 (7)
2416-25.
Journal code: BYG. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY WEEK: 19981204
AB We have studied Ca2+ homeostasis in a unique model of human neurons, the
NT2N cell, which differentiates from a human teratocarcinoma cell line,
NTera2/C1.D1 by retinoic acid treatment. When perifused with Krebs-HEPES
buffer containing 2.5 mM CaCl2, fura-2 loaded NT2N cells produced
spontaneous cytosolic Ca2+ oscillations, or Ca2+ transients. These
cytosolic Ca2+ transients were not blocked by ***antagonists*** of
glutamate (6-cyano-7-nitroquinoxaline-2,3-dione and D(-)-2-amino-5-
phosphonopentanoic acid) or muscarinic (atropine) receptors. Omission of
extracellular Ca2+ completely abolished Ca2+ oscillations and decreased
the average Ca2+ level from 106 +/- 14 nM to 59 +/- 8 nM. Addition of the
L-type Ca2+ channel blocker nifedipine (1 or 10 microM) or of the N-type
inhibitor omega-conotoxin GVIA (5 microM) significantly, although
incompletely, suppressed Ca2+ oscillations, while omega-conotoxin MVIIC (5
microM), a selective ***antagonist*** of P- and Q-channels, had no
effect. Ni2+, at 100 microM, a concentration selective for ***T*** -
type channels, did not inhibit Ca2+ transients. Non-specific
blockage of Ca2+ channels by higher concentrations of Ni2+ (2-5 mM) or
Co2+ (1 mM) abolished Ca2+ oscillations completely. The endoplasmic
reticulum Ca2+-ATPase inhibitor, thapsigargin (1 microM), slightly

decreased Ca2+ oscillation frequency, and induced a small transitory
increase in the average cytosolic Ca2+ concentration. The mRNAs of L-
(alpha1D subunit) and N-type (alpha1B subunit) Ca2+ channel were present
in NT2N cells, while that of a ***T*** - ***type*** Ca2+ channel (***alpha1*** -subunit) was not present in the NT2N cells as shown by
reverse transcription-polymerase chain reaction. In conclusion, NT2N
neuronal cells generate cytosolic Ca2+ oscillations mainly by influx of
extracellular Ca2+ through multiple channels, which include L- and N-type
channels, and do not require activation of glutamate or muscarinic
receptors.

L5 ANSWER 10 OF 21 MEDLINE
DUPLICATE 6
ACCESSION NUMBER: 1999055409 MEDLINE
DOCUMENT NUMBER: 99055409
TITLE: Voltage dependent ***calcium*** ***channels*** in
mammalian spermatozoa.
AUTHOR: Benoff S
CORPORATE SOURCE: Division of Human Reproduction, Department of Obstetrics
and Gynecology, North Shore University Hospital-New York
University School of Medicine, Manhasset, New York 11030,
USA.. sbenoff@nshs.edu
CONTRACT NUMBER: ES 06100 (NIEHS)
SOURCE: FRONTIERS IN BIOSCIENCE, (1998 Dec 1) 3 D1220-40. Ref: 254
Journal code: CUE. ISSN: 1093-4715.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY WEEK: 19990301
AB Calcium influx is an absolute requirement for the physiological acrosome
reaction in sperm from all sources examined, both invertebrate and
mammalian. Pharmacological studies suggest that the major channel in the
sperm head plasma membrane responsible for modulating calcium entry and
intracellular ionized calcium levels could be either an L-type (a class of
high voltage-activated) or a ***T*** - ***type*** (low
voltage-activated) voltage-dependent ***calcium*** ***channel*** .
Patch clamp analysis of calcium currents in immature spermatogenic cells
demonstrates the presence of ***T*** - ***type*** currents.
Therefore, an argument has been put forth that the acrosome reaction of
ejaculated sperm is regulated by a ***T*** - ***type***
calcium ***channel*** . However, indirect analysis of calcium
currents in mature sperm after transfer of ion channels to planar lipid
bilayers detects three current types, including that similar, but not
identical, to an L-type channel, but no ***T*** - ***type***
currents. Molecular cloning of the ***alpha*** - ***1*** pore
forming subunit of ***calcium*** ***channels*** expressed in the
male reproductive tract and in ejaculated sperm has resolved this
controversy, demonstrating the existence of only high voltage-activated
channels. Further analysis of the ***alpha*** - ***1*** subunit
isoform from rat and human testis and sperm suggests that, as a result of
alternate splicing, this L-type ***alpha*** - ***1*** subunit could
produce calcium currents that were T-like, e.g., transient, rapidly
inactivating with slow deactivation. Multiple splice variants of this
isoform were detected in human testis, suggesting a correlation with
intra-individual variation in the ability of sperm to undergo an induced
acrosome reaction and with male infertility. These variants could be
developed as useful biomarkers for susceptibility to environmental and
occupational toxicants. Knowledge of ***calcium*** ***channels***
structure will also contribute to design of new male contraceptives based
on existing ***calcium*** ***channel*** ***antagonists*** .

L5 ANSWER 11 OF 21 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 1998355943 MEDLINE
DOCUMENT NUMBER: 98355943
TITLE: Electrophysiological properties of neonatal rat ventricular
myocytes with ***alpha1*** -adrenergic-induced
hypertrophy.
AUTHOR: Gaughan J P; Hefner C A; Houser S R
CORPORATE SOURCE: Department of Physiology, Temple University School of
Medicine, Philadelphia, Pennsylvania 19140, USA.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Aug) 275 (2 Pt 2) H577-90.
Journal code: 3U8. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
AB The electrophysiology of neonatal rat ventricular myocytes with and
without hypertrophy has not been characterized. The ***alpha1***
-adrenergic ***agonist*** phenylephrine induced hypertrophy in
neonatal rat ventricular myocytes. After 48 h of exposure to 20 microM
phenylephrine, cell surface area of hypertrophied myocytes was 44% larger
than control. Action potential duration was significantly longer in
hypertrophy than in control. There was an increase in L-type Ca2+ current
in control after 48 h in culture, but current density was significantly
less in hypertrophy (-4.7 +/- 0.8 hypertrophy vs. -10.7 +/- 1.2 control
pA/pF, n = 22, P < 0.05). ***T*** - ***type*** Ca2+ current density
was not different. The alpha-adrenergic ***antagonist*** prazosin
blocked the hypertrophy and the chronic effect of phenylephrine on L-type
Ca2+ current. Transient outward K+ current density was decreased 70% in
hypertrophy and was blocked with 4-aminopyridine. No change in Na+ current
density was observed. Staurosporine, a protein kinase C inhibitor,
eliminated the hypertrophy and the effect on L-type Ca2+ current. These
studies showed that phenylephrine-induced hypertrophy occurred via the
alpha1 -adrenergic pathway and caused electrophysiological changes
and effects on ion channel expression.

L5 ANSWER 12 OF 21 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:53497 BIOSIS
DOCUMENT NUMBER: PREV199900053497
TITLE: The safety of ***calcium*** - ***channel*** blockers.
AUTHOR(S): Massie, Barry M. (1)
CORPORATE SOURCE: (1) Univ. Calif. San Francisco, Cardiol. Div., VA Hosp.,
4150 Clement Street, San Francisco, CA 94121 USA
SOURCE: Clinical Cardiology, (Dec., 1998) Vol. 21, No. 12 SUPPL. 2,
pp. II12-II17.
ISSN: 0160-9289.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Calcium*** - ***channel*** blockers are widely used as an
effective treatment for hypertension and angina. Several studies have
raised questions about their safety, suggesting that ***calcium*** -
channel blockers can increase the rates of myocardial infarction
(MI) and death, particularly in patients with heart disease. Reviews of
these studies have uncovered serious methodological shortcomings or have
found them restricted to short-acting drugs, frequently at high doses or
used inappropriately. One study was based on old data regarding only
short-acting nifedipine, which has never been indicated for patients who
have suffered an MI or unstable angina. A case-control study of
short-acting verapamil, diltiazem, and nifedipine suggested an increased
MI rate was confounded by the higher rates of diabetes and preexisting
heart disease in the patients treated with ***calcium*** -
channel blockers. A third study reported significantly decreased
survival only in patients taking short-acting nifedipine; in most of the
cases reported, blood pressure was not controlled. While these studies
alert us to the limitations of short-acting ***calcium*** -
channel blockers and the necessity of considering side effects
such as neurohormonal stimulation, a number of more recent,
better-controlled studies have not confirmed increased risk with
calcium - ***channel*** blockers when appropriately employed.
Calcium - ***channel*** blockers should still be considered
first-line therapy in appropriately selected patients with hypertension or
angina.

L5 ANSWER 13 OF 21 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 96018848 MEDLINE
DOCUMENT NUMBER: 96018848
TITLE: Voltage-dependent blockade of diverse types of
voltage-gated Ca2+ channels expressed in Xenopus oocytes by
the Ca2+ channel ***antagonist*** mibefradil (Ro
40-5967).
AUTHOR: Bezprozvanny I; Tsien R W
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Stanford
University Medical Center, California 94305, USA.
CONTRACT NUMBER: NS24067 (NINDS)
HL07740-02 (NHLBI)
SOURCE: MOLECULAR PHARMACOLOGY, (1995 Sep) 48 (3) 540-9.
Journal code: NGR. ISSN: 0026-895X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199601
AB Four different types of Ca2+ channel ***alpha*** ***1*** subunits,
representing the major classes of voltage-gated Ca2+

channels, were
individually coexpressed along with alpha 2/delta and beta 2b subunits in
Xenopus oocytes. These subunits (and the encoded channel types and major
tissues of origin) included alpha 1C (L-type, cardiac), alpha 1B (N-type,
central nervous system), alpha 1A (P/Q-type, central nervous system), and
alpha 1E (most likely R-type, central nervous system). Divalent cation
currents through these channels (5 mM Ba2+) were evaluated with the
two-microelectrode voltage-clamp technique. The expressed channels were
compared with regard to their responses to a structurally novel,
nondihydropyridine compound, mibefradil (Ro 40-5967). In the micromolar
concentration range, this drug exerted clear inhibitory effects on each of
the four channel types, reducing divalent cation current at all test
potentials, with the non-L-type channels being more sensitive to
inhibition than the L-type channels under fixed experimental conditions.
For all channel types, mibefradil was a much more effective inhibitor at
more depolarized holding potentials, suggesting tighter binding of the
drug to the inactivated state than to the resting state. The difference in
apparent affinities of resting and inactivated states of the channels,
calculated based on a modulated receptor hypothesis, was 30-70-fold. In
addition, the time course of decay of Ca2+ channel current was accelerated
in the presence of drug, consistent with open channel block. The effect of
increasing stimulation frequency was tested for L-type channels and was
found to greatly enhance the degree of inhibition by mibefradil,
consistent with promotion of block by channel opening and inactivation.
Allowing for state-dependent interactions, the drug concentrations found
to block L-, N-, Q-, and R-type channels by 50% are at least 10-fold
higher than half-blocking levels previously reported for ***T*** -
type channels in vascular smooth muscle cells under similar
experimental conditions. This may help explain the ability of the drug to
spare working myocardium (strongly negative resting potential, dominance
of L-type channels in their resting state) while reducing contraction in
blood vessels (presumably involving ***T*** - ***type*** channels or
partially inactivated L-type channels). Thus, mibefradil is a new addition
to the family of nonselective organic Ca2+ channel inhibitors, as
exemplified by bepridil and fluspirilene, and may prove useful as an
experimental tool for studying diverse physiological events initiated by
Ca2+ influx. It complements classes of drugs with relatively selective
effects on L-type channels, as exemplified by nifedipine and diltiazem.

L5 ANSWER 14 OF 21 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 95:30249 SCISEARCH
THE GENUINE ARTICLE: PX343
TITLE: THE CA++-CHANNEL BLOCKER RO-40-5967 BLOCKS DIFFERENTLY ***T*** - ***TYPE*** AND L-TYPE CA++ CHANNELS
AUTHOR: MEHRKE G; ZONG X G (Reprint); FLOCKERZI V; HOFMANN F
CORPORATE SOURCE: TECH UNIV MUNICH, INST PHARMAKOL & TOXIKOL, BIEDERSTEINERSTR 29, D-80802 MUNICH, GERMANY (Reprint); TECH UNIV MUNICH, INST PHARMAKOL & TOXIKOL, D-80802 MUNICH, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (DEC 1994) Vol. 271, No. 3, pp. 1483-1488.
ISSN: 0022-3565.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The effects of Ro 40-5967, a nondihydropyridine Ca++ channel blocker, on low-voltage activated (***T*** - ***type***) and high-voltage activated (L-type) Ca++ channels were compared. L-type barium currents were measured in Chinese hamster ovary cells stably transfected with the ***alpha*** (***1***) subunit of the class Cb Ca++ channel ***T*** - ***type*** barium currents were investigated in human medullary thyroid carcinoma cells. The Ba++ currents of human medullary thyroid carcinoma cells were transient, activated at a threshold potential of -50 mV with the maximum at -14 +/- 3.2 mV and blocked by micromolar Ni++. The T- and L-type current inactivated with time constants of 33.4 +/- 4.1 and 416 +/- 26 msec at maximum barium currents, respectively. Ro 40-5967 inhibited reversibly the T- and L-type currents with IC50 values of 2.7 and 18.6 mu M, respectively. The inhibition of the L-type current was voltage-dependent, whereas that of the ***T*** - ***type*** current was not. Ro 40-5967 blocked ***T*** - ***type*** current already at a holding potential of -100 mV. The different types of block, i.e., voltage-dependent vs, tonic block, may contribute to the pharmacological profile of Ro 40-5967 in intact animals.

L5 ANSWER 15 OF 21 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 95088917 MEDLINE
DOCUMENT NUMBER: 95088917
TITLE: Effects of a new class of calcium ***antagonists*** , SR33557 (fantofarone) and SR33805, on neuronal voltage-activated Ca++ channels.
AUTHOR: Romey G; Lazdunski M
CORPORATE SOURCE: Institut de Pharmacologie Moleculaire et Cellulaire, Valbonne, France..
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1994 Dec) 271 (3) 1348-52.
Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
AB SR33557 (fantofarone) and SR33805 are structurally novel calcium ***antagonists*** that bind selectively to the ***alpha*** ***1*** -subunit of the L-type Ca++ channel at a site distinct from the classical 1,4-dihydrophyridine, phenylalkylamine and benzothiazepine sites but in allosteric interactions with them. Blocking effects of fantofarone and SR33805 on the different types of voltage-activated Ca++ currents have been investigated with the whole-cell patch-clamp method in chick dorsal root ganglion neurons (for T-, L- and N-type currents) and in rat cerebellar Purkinje neurons (for P-type current) in primary culture. Neuronal L-type Ca++ channels are blocked totally by fantofarone and SR33805 in the microM range of concentration as in skeletal muscle and cardiac cells at a holding membrane potential of -80 mV. The sequence of efficacy is SR33805 (IC50 = 26 nM) > fantofarone (IC50 = 0.35 microM). N- and P-type channels are not very sensitive to fanto-farone and SR33805 (IC50 approximately 5 microM). The ***T*** - ***type*** channel is not affected by these drugs.

L5 ANSWER 16 OF 21 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95005636 EMBASE
DOCUMENT NUMBER: 1995005636
TITLE: [Molecular diversity of ***calcium*** ***channels***: From gene to function]. DIVERSITE MOLECULAIRE DES CANAUX CALCIQUES: DU GENE A LA FONCTION.
AUTHOR: Nargeot J.; Charnet P.
CORPORATE SOURCE: Ct. Rech. Biochimie Macromoleculaire, Cnrs UPR 9008, Inserm U. 249, BP 5051,34033 Montpellier, France
SOURCE: Medecine/Sciences, (1994) 10/12 (1293-1308).
ISSN: 0767-0974 CODEN: MSMSE4
COUNTRY: France
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: French; English
AB Recent studies have revealed the molecular and functional diversity of voltage-gated ***calcium*** ***channels*** . Electrophysiological and pharmacological experiments on various cell types have provided a way of characterizing a Low Voltage Activated (LVA) or ' ***T*** - ***type*** ', and several High Voltage Activated (HVA) ***calcium*** ***channels*** . LVA Ca2+ channels have fast kinetics and no specific ligands while HVA Ca2+ channels have been identified mainly by the use of specific toxins, and named L, N, P and Q. They are blocked by dihydropyridines, .omega.-CgT-GVIA, .omega.-Aga-IVA and .omega.-CmT-MVIIC, respectively. Biochemical studies have revealed that skeletal muscle Ca2+ channels are composed of a pore-forming . ***alpha*** . ***1*** subunit and several associated subunits (.alpha.2-.delta., .beta. and .gamma.). Several . ***alpha*** . ***1*** subunits have been cloned from various tissues and are encoded by at least six genes. Their expression in Xenopus oocytes or in mammalian cells induces ***calcium*** ***channel*** currents, the properties of which seem to correspond to the different Ca2+ channels identified in various cells. However, it has been suggested that further diversity may be provided by the addition of auxiliary subunits and particularly the .beta. subunits which are thought to be associated to most of the 9a1 subunits. .beta. subunits encoded by at least four genes (.beta.1, .beta.2, .beta.3, .beta.4) expressed in the nervous system and other tissues enhance Ca2+ channel activity and are able to modify both electrophysiological and pharmacological properties. However, a differential

effect on calcium
current inactivation has been observed between the different isoforms
(.beta.1, .beta.2, .beta.3) and their splice variants (.beta.1a, .beta.1b)
indicating that multiple Ca2+ channel gating may arise from the expression
of different subtypes of .beta. subunits. The implication of Ca2+ channels
in pathophysiology has been recently suggested and the genes coding for .
alpha . ***1*** or .beta. subunits are potential candidates in
some pathologies. Several autoimmune diseases have also been suggested to
involve Ca2+ channels as the targets for antibodies. Moreover, the
functional diversity of neuronal Ca2+ channel offers new perspectives in
the development of drugs for the treatment of neurologic disorders.

L5 ANSWER 17 OF 21 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 95055196 MEDLINE
DOCUMENT NUMBER: 95055196
TITLE: The L-type ***calcium*** ***channel*** current is
increased by ***alpha*** - ***1*** adrenoceptor
activation in neonatal rat ventricular cells.
AUTHOR: Liu Q Y; Karpinski E; Pang P K
CORPORATE SOURCE: Department of Physiology, University of Alberta, Edmonton,
Canada..
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS,
(1994 Nov) 271 (2) 935-43.
Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
AB The activation of ***alpha*** - ***1*** adrenoceptors in adult rat
ventricular cells results in the reduction of the transient outward K+
current, but does not affect Ca++ currents. In this study, using neonatal
rat ventricular cells, the ***alpha*** - ***1*** adrenergic receptor
agonist phenylephrine increased the long-lasting (L-type) Ca++
channel current (dihydropyridine-sensitive) and the increase was
concentration-dependent. Phenylephrine did not, however, modulate the
transient-type (***T*** - ***type***) Ca++ channel current. The
alpha - ***1*** effect of phenylephrine was reversed or
abolished by prazosin, an ***alpha*** - ***1*** ***antagonist***
. The alpha-2 ***agonist*** clonidine had no effect on the L-type
current. Yohimbine, an alpha-2 ***antagonist*** , and propranolol, a
beta ***antagonist*** , did not inhibit the effect of phenylephrine on
L-type current. The effect of phenylephrine was abolished by pretreatment
with WB4101, an alpha-1A ***antagonist*** , but not by
chloroethylclonidine, an alpha-1B ***antagonist*** . In addition,
norepinephrine also increased the L-type current in the presence of
propranolol and this effect was reversed by washout. These observations
suggest that phenylephrine increased the L-type Ca++ channel current
specifically through the activation of alpha-1A adrenergic receptors in
neonatal rat ventricular myocytes. This may explain in part the increase
in the plateau phase of the action potential and the positive inotropic
response of the neonatal myocardium to phenylephrine. This is the first
description of an increase in L-type Ca++ current by alpha-1A adrenoceptor
activation in neonatal rat ventricular myocytes, and this effect is
different from that reported in adult rat myocytes.

L5 ANSWER 18 OF 21 MEDLINE
DUPLICATE 11
ACCESSION NUMBER: 95121362 MEDLINE
DOCUMENT NUMBER: 95121362
TITLE: Effects of two chemically related new Ca2+ channel
antagonists , SR33557 (fantofarone) and SR33805, on
the L-type cardiac channel.
AUTHOR: Romey G; Bois P; Lazdunski M
CORPORATE SOURCE: Institut de Pharmacologie Molecculaire et Cellulaire, Sophia
Antipolis, Valbonne, France..
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1994 Sep 22) 263 (1-2)
101-5.
Journal code: EN6. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
AB Fantofarone (SR33557) is a substituted indolizine and SR33805 is a
substituted indole. These drugs have been shown to specifically bind to
the ***alpha*** ***1*** subunit of the L-type Ca2+ channel at the
same site, distinct from those of the classical 1,4-dihydropyridine,
phenylalkylamine or benzothiazepine Ca2+ ***antagonists*** , but in
negative allosteric interaction with them. The present work shows that
fantofarone and SR33805 block L-type but not ***T*** - ***type***
Ca2+ channels in mouse cardiac cells in primary culture. This block is
voltage-dependent. Fantofarone and SR33805 are potent Ca2+ channel
blockers in depolarized conditions (i.e. at a holding potential of -40 mV)
with an EC50 = 1.4 and 4.1 nM, respectively. In polarized conditions (i.e.
at a holding potential of -80 mV), SR33805 is a better Ca2+ channel
blocker (EC50 = 33 nM) than fantofarone (EC50 = 0.15 microM). Therefore
differences in their chemical structures make the blocking action of
fantofarone more sensitive to voltage than that of SR33805.

L5 ANSWER 19 OF 21 MEDLINE
DUPLICATE 12
ACCESSION NUMBER: 94150810 MEDLINE
DOCUMENT NUMBER: 94150810
TITLE: Distinctive pharmacology and kinetics of cloned neuronal
Ca2+ channels and their possible counterparts in mammalian
CNS neurons.
AUTHOR: Zhang J F; Randall A D; Ellinor P T; Horne W A; Sather W A;
Tanabe T; Schwarz T L; Tsien R W
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Stanford
University Medical Center, CA 94305.
CONTRACT NUMBER: GM42376 (NIGMS)
NS24067 (NINDS)
SOURCE: NEUROPHARMACOLOGY, (1993 Nov) 32 (11) 1075-88. Ref: 40
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
AB This paper provides a brief overview of the diversity of voltage-gated Ca2+ channels and our recent work on neuronal Ca2+ channels with novel
pharmacological and biophysical properties that distinguish them from L,
N, P or ***T*** - ***type*** channels. The Ca2+ channel
alpha ***1*** subunit known as alpha 1A or BI [Mori Y.,
Friedrich T., Kim M.-S., Mikami A., Nakai J., Ruth P., Bosse E., Hofmann
F., Flockerzi V., Furuichi T., Mikoshiba K., Imoto K., Tanabe T. and Numa
S. (1991) Nature 350, 398-402] is generally assumed to encode the P-type
Ca2+ channel. However, we find that alpha 1A expressed in Xenopus oocytes
differs from P-type channels in its kinetics of inactivation and its
degree of sensitivity to block by the peptide toxins omega-Aga-IVA and
omega-CTx-MVIIC [Sather W. A., Tanabe T., Zhang J.-F., Mori Y., Adams M.
E. and Tsien R. W. (1993) Neuron 11, 291-303]. Thus, alpha 1A is capable
of generating a Ca2+ channel with characteristics quite distinct from
P-type channels. Doe-1, recently cloned from the forebrain of a marine
ray, is another ***alpha*** ***1*** subunit which exemplifies a
different branch of the Ca2+ channel family tree [Horne W. A., Ellinor P.
T., Inman I., Zhou M., Tsien R. W. and Schwarz T. L. (1993) Proc. Natn.
Acad. Sci. U.S.A. 90, 3787-3791]. When expressed in Xenopus oocytes, doe-1
forms a high voltage-activated (HVA) Ca2+ channel [Ellinor P. T., Zhang
J.-F., Randall A. D., Zhou M., Schwarz T. L., Tsien R. W. and Horne W.
(1993) Nature 363, 455-458]. It inactivates more rapidly than any
previously expressed ***calcium*** ***channel*** and is not
blocked by dihydropyridine ***antagonists*** or omega-Aga-IVA. Doe-1
current is reduced by omega-CTx-GVIA, but the inhibition is readily
reversible and requires micromolar toxin, in contrast to this toxin's
potent and irreversible block of N-type channels. Doe-1 shows considerable
sensitivity to block by Ni2+ or Cd2+. We have identified components of
Ca2+ channel current in rat cerebellar granule neurons with kinetic and
pharmacological features similar to alpha 1A and doe-1 in oocytes [Randall
A. D., Wendland B., Schweizer F., Miljanich G., Adams M. E. and Tsien R.
W. (1993) Soc. Neurosci. Abstr. 19, 1478]. The doe-1-like component
(R-type current) inactivates much more quickly than L, N or P-type
channels, and also differs significantly in its pharmacology.(ABSTRACT
TRUNCATED AT 400 WORDS)

L5 ANSWER 20 OF 21 MEDLINE
ACCESSION NUMBER: 89130135 MEDLINE
DOCUMENT NUMBER: 89130135
TITLE: Modulation of ***calcium*** ***channels*** in
cardiac and neuronal cells by an endogenous peptide.
AUTHOR: Callewaert G; Hanbauer I; Morad M
CORPORATE SOURCE: Department of Physiology, School of Medicine, University of
Pennsylvania, Philadelphia 19104.
CONTRACT NUMBER: HL16152 (NHLBI)
SOURCE: SCIENCE, (1989 Feb 3) 243 (4891) 663-6.
Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198905

AB ***Calcium*** ***channels*** mediate the generation of action
potentials, pacemaking, excitation-contraction coupling, and secretion and
signal integration in muscle, secretory, and neuronal cells. The
physiological regulation of the L-type ***calcium*** ***channel***
is thought to be mediated primarily by guanine nucleotide-binding proteins
(G proteins). A low molecular weight endogenous peptide has been isolated
and purified from rat brain. This peptide regulates up and down the
cardiac and neuronal ***calcium*** ***channels*** , respectively.
In cardiac myocytes, the peptide-induced enhancement of the L-type calcium
current had a slow onset (half-time approximately 75 seconds), occurred
via a G protein-independent mechanism, and could not be inhibited by
alpha ***1*** -adrenergic, beta-adrenergic, or angiotensin II
blockers. In neuronal cells, on the other hand, the negative effect had a
rapid onset (half-time less than 500 milliseconds) and was observed on
both ***T*** - ***type*** and L-type ***calcium***
channels .

L5 ANSWER 21 OF 21 MEDLINE
ACCESSION NUMBER: 89301359 MEDLINE
DOCUMENT NUMBER: 89301359
TITLE: ***Calcium*** ***channels*** reconstituted from the
skeletal muscle dihydropyridine receptor protein complex
and its ***alpha*** ***1*** peptide subunit in
lipid bilayers.
AUTHOR: Pelzer D; Grant A O; Cavalie A; Pelzer S; Sieber M; Hofmann
F; Trautwein W
CORPORATE SOURCE: II. Physiologisches Institut, Medizinische Fakultat,
Universitat des Saarlandes, Homburg/Saar, Federal Republic
of Germany.
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1989) 560
138-54.
Journal code: 5NM. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198910
AB In the first part of this study, we show that sDHPR and pDHPR preparations
reconstituted into lipid bilayers formed on the tips of patch pipettes
exhibit two divalent cation-selective conductance levels of 9 and 20 pS,
similar in single-channel conductance to VSCC reported in a variety of
intact preparations (see Pelzer et al. and Tsien et al. for review). The
larger conductance level is similar to the VSCC identified in intact rat
t-tubule membranes and described in sDHPR and pDHPR preparations, and
shares many properties in common with activity from L-type VSCC. It is
sensitive to augmentation by the DHP ***agonist*** (+/-)-BAY K 8644
and cAMP-dependent phosphorylation, and to block by the phenylalkylamine
(+/-)-D600 and the inorganic blocker CoCl2. Its open-state probability and
open times are increased upon depolarization as expected for a
voltage-dependent activation process. Upon depolarization beyond the
reversal potential, however, open-state probability and open times decline
again. A reasonable way to explain the bell-shaped dependence of open
times and open-state probability on membrane potential is to assume
voltage-dependent ion-pore interactions that produce closing of the
channel at strong negative and positive membrane potentials. By contrast,
the smaller conductance level may be similar to the 10.6-pS t-tubule VSCC
described by Rosenberg et al. and may best be compared with ***T*** -
type VSCC. It is largely resistant to augmentation by (+/-)-BAY K
8644 and cAMP-dependent phosphorylation or block by (+/-)-D600, but is
sensitive to block by CoCl2. Its open times and open-state probability
show a sole dependence on membrane potential where depolarization
increases both parameters sigmoidally from close to zero up to a
saturating level. Both elementary conductance levels do not exhibit
significant inactivation over a wide potential range, which may suggest
that skeletal muscle VSCC inactivation is either poorly or not
voltage-dependent at all. This possibility seems in agreement with bilayer
recordings on reconstituted intact t-tubule membranes and voltage-clamp
recordings on intact fibers. It supports the idea that the decline of Ca2+
current in intact skeletal muscle fibers may be due to Ca2+ depletion from
the t-tubule system and/or to inactivation induced by Ca2+ release from
the sarcoplasmic reticulum. We consistently observe two conductance levels
of 9 and 20 pS, either singly, or together in the same bilayer from
solubilized DHPR samples and even highly purified DHPR
preparations.(ABSTRACT TRUNCATED AT 400 WORDS)

=> d his

(FILE 'HOME' ENTERED AT 10:11:34 ON 22 FEB 2001)

FILE 'MEDLINE, JAPIO, BIOSIS, SCISEARCH, WPIDS, CAPLUS, EMBASE' ENTERED
AT 10:11:43 ON 22 FEB 2001
L1 141663 S CALCIUM CHANNEL#
L2 3515 S L1 AND (T-TYPE OR T TYPE)
L3 216 S L2 AND (ALPHA-1 OR ALPHA 1 OR ALPHA1)
L4 51 S L3 AND (AGONIST# OR ANTAGONIST#)
L5 21 DUP REM L4 (30 DUPLICATES REMOVED)
L6 104 DUP REM L3 (112 DUPLICATES REMOVED)

=> d l6 ibib abs 1-104

L6 ANSWER 1 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2001:83752 SCISEARCH
THE GENUINE ARTICLE: 392UL
TITLE: Alternative splicing in intracellular loop connecting
domains II and III of the ***alpha*** (***1***)
subunit of Ca(v)1.2 Ca2+ channels predicts two-domain
polypeptides with unique C-terminal tails
AUTHOR: Wielowieyski P A; Wigle J T; Salih M; Hum P; Tuana B S
(Reprint)
CORPORATE SOURCE: Univ Ottawa, Dept Cellular & Mol Med, 451 Smyth Rd,
Ottawa, ON K1H 8H5, Canada (Reprint); Univ Ottawa, Dept
Cellular & Mol Med, Ottawa, ON K1H 8M5, Canada
COUNTRY OF AUTHOR: Canada
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (12 JAN 2001) Vol. 276,
No. 2, pp. 1398-1406.
Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC,
9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.
ISSN: 0021-9258.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 70
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Novel splice variants of the Lu, subunit of the Ca(v)1.2 voltage-gated
Ca2+ channel were identified that predicted two truncated forms of the or,
subunit comprising domains I and II generated by alternative splicing in
the intracellular loop region linking domains II and III. In rabbit heart
splice variant 1 (RH-1), exon 19 was deleted, which resulted in a reading
frameshift of exon 20 with a premature termination codon and a novel
19-amino acid carboxyl-terminal tail. In the RH-2 variant, exons 17 and 18
were deleted, leading to a reading frameshift of exons 19 and 20 with a
premature stop codon and a novel 62-amino acid carboxyl-terminal tail.
RNase protection assays with RH-1 and RH-2 cRNA probes confirmed the
expression in cardiac and neuronal tissue but not skeletal muscle. The
deduced amino acid sequence from full-length cDNAs encoding the two
variants predicted polypeptides of 99.0 and 99.2 kDa, which constituted
domains I and II of the ***alpha*** (***1***), subunit of the
Ca(v)1.2 channel. Antipeptide antibodies directed to sequences in the
second intracellular loop between domains II and III identified the
240-kDa Ca(v)1.2 subunit in sarcolemmal and heavy sarcoplasmic reticulum
(HSR) membranes and a 99-kDa polypeptide in the HSR, An antipeptide
antibody raised against unique sequences in the RH-2 variant also
identified a 99-kDa polypeptide in the HSR. These data reveal the
expression of additional Ca2+ channel structural units generated by
alternative splicing of the Ca(v)1.2 gene.

L6 ANSWER 2 OF 104 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-271475 [23] WPIDS
DOC. NO. CPI: C2000-082967
TITLE: Novel nucleic acids encoding pancreatic ***T*** -
type ***calcium*** ***channels*** used
for regulation of ***T*** - ***type***
calcium ***channels*** and treatment of type
II diabetes.
DERWENT CLASS: B04 D16
INVENTOR(S): LI, M
PATENT ASSIGNEE(S): (SALA-N) SOUTH ALABAMA MEDICAL SCI FOUND
COUNTRY COUNT: 83
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000015845	A1	20000323	(200023)*	EN	124

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
OA PT SD SE SL SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
GE GH GM HR HU ID IL IN IS JP KE KG KP

KR KZ LC LK LR LS LT LU LV
MD MG MK MN MW MX NO NZ PL PT RO
RU SD SE SG SI SK SL TJ TM TR TT
UA UG UZ VN YU ZW
AU 9960217 A 20000403 (200034)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 2000015845 A1		WO 1999-US19675 19990826
AU 9960217 A		AU 1999-60217 19990826

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9960217 A	Based on	WO 200015845

PRIORITY APPLN. INFO: US 1999-117399 19990127; US 1998-98004 19980826
AN 2000-271475 [23] WPIDS
AB WO 200015845 A UPAB: 20000516
NOVELTY - An isolated pancreatic ***T*** - ***type***
calcium ***channel*** (I) is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) an isolated nucleic acid molecule (NAM) (II) encoding (I);
(2) an antisense NAM (III) complementary to (II);
(3) a cell comprising (III);
(4) an expression vector comprising (III);
(5) a method (A) of decreasing expression of a (I) in a host cell;
(6) a ribozyme (IV) having a recognition sequence complementary to a portion of (II);
(7) a cell comprising (IV);
(8) an expression vector comprising (IV);
(9) a cell comprising (II);
(10) an expression vector comprising (II);
(11) a method (B) of increasing expression of (II) in a host cell, comprising introducing (I) into the cell;
(12) a method (C) of screening a substance for the ability to modify the function of (I);
(13) a method (D) of obtaining DNA encoding (II)
(14) a DNA oligomer capable of hybridizing to (I);
(15) a method (E) of detecting presence of a pancreatic ***T*** - ***type*** ***calcium*** ***channel*** in a sample,
(16) an antibody (V) specific for (II); and
(17) a method of detecting the presence of (I) in a sample, comprising contacting the sample with (V) and detecting the complex formed.
ACTIVITY - antidiabetic.
MECHANISM OF ACTION - The polypeptide functions as a pancreatic ***T*** - ***type*** ***calcium*** ***channel*** .
USE - The pancreatic ***T*** - ***type*** ***calcium*** ***channel*** polynucleotides and polypeptides are used for treating diseases associated with abnormal expression or function of ***T*** - ***type*** ***calcium*** ***channels*** . They are especially used for treating type II diabetes (claimed). They are used in methods for modifying insulin secretion by pancreatic beta cells, for modifying basal calcium levels in cells, for modifying the action of potential L type ***calcium*** ***channels*** in cells, for modifying pancreatic cell death, for modifying pancreatic beta cell proliferation, and for modifying calcium influx through L type ***calcium*** ***channels*** in cells (all claimed). The polypeptides are used to produce antibodies, which can be used in assays to identify cells or tissues which express pancreatic ***T*** - ***type*** ***calcium*** ***channels*** , or for detecting pancreatic ***T*** - ***type*** ***calcium*** ***channels*** in samples. Antisense sequences and ribozymes can be used to decrease expression of pancreatic ***T*** - ***type*** ***calcium*** ***channels*** . Inhibitors and antagonists (identified using the polypeptides of the invention) can be used to decrease the activity of pancreatic ***T*** - ***type*** ***calcium*** ***channels*** .
ADVANTAGE - No stated advantage given in the specification.
DESCRIPTION OF DRAWING(S) - The figure is a schematic illustration representing the partial rat genomic nucleotide composition between domains III and IV. Genomic DNA contained an exon specific to alpha 1G (shaded circle) and an exon specific to the ***alpha*** ***1*** subunit of ***T*** - ***type*** Ca2+ deduced from INS-1 (shaded rectangle). Other exons (open rectangles) are identical between the two cDNAs. The bold letters indicate the nucleotide coding Gly1667.
Dwg.1b/25

L6 ANSWER 3 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:334427 BIOSIS
DOCUMENT NUMBER: PREV200000334427
TITLE: Molecular and functional properties of the human alpha1G subunit that forms ***T*** - ***type*** ***calcium*** ***channels*** .
AUTHOR(S): Monteil, Arnaud; Chemin, Jean; Bourinet, Emmanuel; Mennessier, Gerard; Lory, Philippe (1); Nargeot, Joel
CORPORATE SOURCE: (1) IGH-CNRS UPR 1142, 141 rue de la Cardonille, F-34396, Montpellier cedex, 05 France
SOURCE: Journal of Biological Chemistry, (March 3, 2000) Vol. 275, No. 9, pp. 6090-6100. print.
ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB We describe here several novel properties of the human alpha1G subunit that forms ***T*** - ***type*** ***calcium*** ***channels*** . The partial intron/exon structure of the corresponding gene CACNA1G was defined and several alpha1G isoforms were identified, especially two isoforms that exhibit a distinct III-IV loop: alpha1G-a and alpha1G-b. Northern blot and dot blot analyses indicated that alpha1G mRNA is predominantly expressed in the brain, especially in thalamus, cerebellum, and substantia nigra. Additional experiments have also provided evidence that alpha1G mRNA is expressed at a higher level during fetal life in nonneuronal tissues (i.e. kidney, heart, and lung). Functional expression in HEK 293 cells of a full-length cDNA encoding the shortest alpha1G isoform identified to date, alpha1G-b, resulted in transient, low threshold activated Ca2+ currents with the expected permeability ratio (ISr > ICa gtoreq IBa) and channel conductance (apprx7 pS). These properties, together with slowly deactivating tail currents, are typical of those of native ***T*** - ***type*** Ca2+ channels. This alpha1G-related current was inhibited by mibefradil (IC50 = 2 muM) and weakly blocked by Ni2+ ions (IC50 = 148 muM) and amiloride (IC50 > 1 mM). We showed that steady state activation and inactivation properties of this current can generate a "window current" in the range of -65 to -55 mV. Using neuronal action potential waveforms, we show that alpha1G channels produce a massive and sustained Ca2+ influx due to their slow deactivation properties. These latter properties would account for the specificity of Ca2+ influx via ***T*** - ***type*** channels that occurs in the range of physiological resting membrane potentials, differing considerably from the behavior of other Ca2+ channels.

L6 ANSWER 4 OF 104 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000122674 EMBASE
TITLE: pH modification of human ***T*** - ***type*** ***calcium*** ***channel*** gating.
AUTHOR: Delisle B.P.; Satin J.
CORPORATE SOURCE: B.P. Delisle, Dept. of Physiology, MS-508, Univ. of Kentucky Coll. of Medicine, Lexington, KY 40536-0298, United States. bpdeli00@pop.uky.edu
SOURCE: Biophysical Journal, (2000) 78/4 (1895-1905).
Refs: 42
ISSN: 0006-3495 CODEN: BIOJAU
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB External pH (pH(o)) modifies ***T*** - ***type*** ***calcium*** ***channel*** gating and permeation properties. The mechanisms of ***T*** - ***type*** channel modulation by pH remain unclear because native currents are small and are contaminated with L- type calcium currents. Heterologous expression of the human cloned ***T*** - ***type*** channel, .alpha.1H, enables us to determine the effect of changing pH on isolated ***T*** - ***type*** calcium currents. External acidification from pH(o) 8.2 to pH(o) 5.5 shifts the midpoint potential (V(1/2)) for steady-state inactivation by 11 mV, shifts the V(1/2) for maximal activation by 40 mV, and reduces the voltage dependence of channel activation. The .alpha.1H reversal potential (E(rev)) shifts from +49 mV at pH(o) 8.2 to +36 mV at pH(o) 5.5. The maximal macroscopic conductance (G(max)) of . ***alpha*** . ***1*** H increases at pH(o) 5.5 compared to pH(o) 8.2. The E(rev) and G(max) data taken together suggest that external protons decrease calcium/monovalent ion relative permeability. In response to a sustained depolarization .alpha.1H currents inactivate with a single exponential function. The macroscopic inactivation time constant is a steep function of voltage for potentials < -30 mV at pH(o) 8.2. At pH(o) 5.5 the voltage dependence of .tau.(inact)

shifts more depolarized, and is also a more gradual function of voltage.
The macroscopic deactivation time constant (.tau.(deact)) is a function of
voltage at the potentials tested. At pH(o) 5.5 the voltage dependence of
.tau.(deact) is simply transposed by .apprx.40 mV, without a concomitant
change in the voltage dependence. Similarly, the delay in recovery from
inactivation at V(rec) of -80 mV in pH(o) 5.5 is similar to that with a
V(rec) of -120 mV at pH(o) 8.2. We conclude that .alpha.1H is uniquely
modified by pH(o) compared to other ***calcium*** ***channels*** .
Protons do not block .alpha.1H current. Rather, a proton-induced change in
activation gating accounts for most of the change in current magnitude
with acidification.

L6 ANSWER 5 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:240714 BIOSIS
DOCUMENT NUMBER: PREV200000240714
TITLE: Regulation of the ***calcium*** ***channel*** alpha1G subunit by divalent cations and organic blockers.
AUTHOR(S): Lacinova, L. (1); Klugbauer, N.; Hofmann, F.
CORPORATE SOURCE: (1) Institut fuer Pharmakologie und Toxikologie, Technischen Universitaet Muenchen, Biedersteiner Str. 29, 80802, Muenchen Germany
SOURCE: Neuropharmacology, (April 27, 2000) Vol. 39, No. 7, pp. 1254-1266. ISSN: 0028-3908.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The pharmacological properties of the expressed murine ***T*** ***type*** alpha1G channel were characterized using the whole cell patch
clamp configuration. Ba2+ or Ca2+ were used as charge carriers. Both IBa
and ICa were blocked by Ni2+ and Cd2+ with IC50 values of 0.47+-0.04 and
1.13+-0.06 mM (Ni2+) and 162+-13 and 658+-23 muM (Cd2+), respectively.
Ni2+, but not Cd2+, modified the gating of channel activation. Ni2+
consistently accelerated channel deactivation while Cd2+ had a similar
effect only on ICa. The alpha1G channel was potently blocked by mibefradil
in a dose- and voltage-dependent manner. IBa was moderately blocked by
phenytoin (IC50 73.9+-1.9 muM) and was resistant to the block by
valproate. Also 3 mM ethosuximide blocked 20 and 35% of the IBa at a HP of
-100 and -60 mV, respectively, while 5 mM amiloride inhibited IBa by 38%
and significantly slowed current activation. The alpha1G channel was not
affected by 10 muM tetrodotoxin. Both 1 muM (+)isradipine and 10 muM
nifedipine inhibited 18 and 14% of IBa amplitude at a HP of -100 mV, and
23% and 29% of IBa amplitude at a HP of -60 mV, respectively. The alpha1G
current was minimally activated by 1 muM Bay K 8644.

L6 ANSWER 6 OF 104 MEDLINE
ACCESSION NUMBER: 2000225542 MEDLINE
DOCUMENT NUMBER: 20225542
TITLE: Neuronal distribution and functional characterization of the ***calcium*** ***channel*** alpha2delta-2 subunit.
AUTHOR: Hobom M; Dai S; Marais E; Lacinova L; Hofmann F; Klugbauer N
CORPORATE SOURCE: Institut fur Pharmakologie und Toxikologie der Technischen Universitat Munchen, Germany.
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (2000 Apr) 12 (4) 1217-26. Journal code: BYG. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY WEEK: 20000804
AB The auxiliary ***calcium*** ***channel*** alpha2delta subunit
comprises a family of three genes, alpha2delta-1 to 3, which are expressed
in a tissue-specific manner. alpha2delta-2 mRNA is found in the heart,
skeletal muscle, brain, kidney, liver and pancreas. We report here for the
first time the identification and functional characterization of
alpha2delta-2 splice variants and their mRNA distribution in the mouse
brain. The splice variants differ in the alpha2 and delta protein by eight
and three amino acid residues, respectively, and are differentially
expressed in cardiac tissue and human medullary thyroid carcinoma (hMTC)
cells. In situ hybridization of mouse brain sections revealed the highest
expression of alpha2delta-2 mRNA in the Purkinje cell layer of the
cerebellum, habenulae and septal nuclei, and a lower expression in the
cerebral cortex, olfactory bulb, thalamic and hypothalamic nuclei, as well
as the inferior and superior colliculus. As the in situ data did not
suggest a specific colocalization with any ***alpha1*** subunit,
coexpression studies of alpha2delta-2 were carried out either with the
high-voltage-gated ***calcium*** ***channels*** , alpha1C, alpha1E
or alpha1A, or with the low-voltage-gated ***calcium*** ***channel*** , alpha1G. Coexpression of alpha2delta-2 increased the
current density, shifted the voltage dependence of channel activation and
inactivation of alpha1C, alpha1E and alpha1A subunits in a hyperpolarizing
direction, and accelerated the decay and shifted the steady-state
inactivation of the alpha1G current.

L6 ANSWER 7 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:50967 BIOSIS
DOCUMENT NUMBER: PREV200100050967
TITLE: The alpha1G-subunit of a voltage-dependent Ca2+ channel is localized in rat distal nephron and collecting duct.
AUTHOR(S): Andreasen, Ditte; Jensen, Boye L. (1); Hansen, Pernille B.; Kwon, Tae-Hwan; Nielsen, Soren; Skott, Ole
CORPORATE SOURCE: (1) Dept. of Physiology and Pharmacology, Winslowparken 21.3, DK-5000, Odense C: bljensen@health.sdu.dk Denmark
SOURCE: American Journal of Physiology, (December, 2000) Vol. 279, No. 6 Part 2, pp. F997-F1005. print. ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The molecular type and localization of ***calcium*** ***channels*** along the nephron are not well understood. In the present study, we
assessed the distribution of the recently identified alpha1G-subunit
encoding a voltage-dependent ***calcium*** ***channel*** with
T - ***type*** characteristics. Using a RNase protection assay,
alpha1G-mRNA levels in kidney regions were determined as inner medulla
mchgt outer medulla simeq cortex. RT-PCR analysis of microdissected rat
nephron segments revealed alpha1G expression in the distal convoluted
tubule (DCT), in the connecting tubule and cortical collecting duct
(CT+CCD), and inner medullary collecting duct (IMCD). alpha1G mRNA was
expressed in the IMCD cell line mIMCD-3. Single- and double-labeling
immunohistochemistry and confocal laser microscopy on semithin paraffin
sections of rat kidneys by using an anti-alpha1G antibody demonstrated a
distinct labeling at the apical plasma membrane domains of DCT cells, CT
principal cells, and IMCD principal cells.

L6 ANSWER 8 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:417290 SCISEARCH
THE GENUINE ARTICLE: 319EW
TITLE: Immunodetection of alpha 1E voltage-gated Ca2+ channel in chromogranin-positive muscle cells of rat heart, and in distal tubules of human kidney
AUTHOR: Weiergraber M; Pereverzev A; Vajna R; Henry M; Schramm M; Nastainczyk W; Grabsch H; Schneider T (Reprint)
CORPORATE SOURCE: UNIV COLOGNE, INST NEUROPHYSIOL, ROBERT KOCH STR 39, D-50931 COLOGNE, GERMANY (Reprint); UNIV COLOGNE, INST NEUROPHYSIOL, D-50931 COLOGNE, GERMANY; UNIV SAARLAND, INST MED BIOCHEM & MOL BIOL, D-6650 HOMBURG, GERMANY; UNIV DUSSELDORF, INST PATHOL, D-4000 DUSSELDORF, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY, (JUN 2000) Vol. 48, No. 6, pp. 807-819. Publisher: HISTOCHEMICAL SOC INC, UNIV WASHINGTON, DEPT BIOSTRUCTURE, BOX 357420, SEATTLE, WA 98195. ISSN: 0022-1554.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 62
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The ***calcium*** ***channel*** alpha 1E subunit was originally
cloned from mammalian brain. A new splice variant was recently identified
in rat islets of Langerhans and in human kidney by the polymerase chain
reaction. The same isoform of alpha 1E was detected in rat and guinea pig
heart by amplifying indicative cDNA fragments and by immunostaining using
peptide-specific antibodies. The apparent molecular size of cardiac alpha
1E was determined by SDS-PAGE and immunoblotting (218 +/- 6 kD; n = 3).
Compared to alpha 1E from stably transfected HEK-293 cells, this is
smaller by 28 kD. The distribution of alpha 1E in cardiac muscle cells of
the conducting system and in the cardiomyoblast cell line H9c2 was
compared to the distribution of chromogranin, a marker of neuroendocrine
cells, and to the distribution of atrial natriuretic peptide (ANP). In
serial sections from atrial and ventricular regions of

rat heart,
co-localization of alpha 1E with ANP was detected in atrium and with
chromogranin A/B in Purkinje fibers of the conducting system in both rat
atrium and ventricle. The kidney is another organ in which natriuretic
peptide hormones are secreted. The detection of alpha 1E in the distal
tubules of human kidney, where urodilatin is stored and secreted, led to
the conclusion that the expression of alpha 1E in rat heart and human
kidney is linked to regions with endocrine functions and therefore is
involved in the Ca2+-dependent secretion of peptide hormones such as ANP
and urodilatin.

L6 ANSWER 9 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
ACCESSION NUMBER: 2000:447682 BIOSIS
DOCUMENT NUMBER: PREV200000447682
TITLE: Influence of ***T*** - ***type*** Ca2+ (mibefradil)
and Cl- (indanyloxyacetic acid 94) channel antagonists on
alpha1 -adrenoceptor mediated contractions in rat
aorta.
AUTHOR(S): Duggan, Jennifer A.; Tabrizchi, Reza (1)
CORPORATE SOURCE: (1) Division of Basic Medical Sciences, Faculty of
Medicine, Memorial University of Newfoundland, Saint
John's, NF, A1B 3V6 USA
SOURCE: Canadian Journal of Physiology and Pharmacology,
(September, 2000) Vol. 78, No. 9, pp. 714-720. print.
ISSN: 0008-4212.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English; French
AB The effects of the ***T*** - ***type*** and L-type Ca2+ channel
antagonists, mibefradil and nifedipine, respectively, and those of a Cl-
channel antagonist, indanyloxyacetic acid 94, on mechanical responses
elicited by selective activation of ***alpha1*** -adrenoceptors using
cirazoline were examined in rat isolated aortic rings. The presence of
mibefradil (300 nM), indanyloxyacetic acid, 94 (30 muM) and nifedipine
(300 nM) alone inhibited mechanical responses elicited by cirazoline. The
concentration-response curves to cirazoline were displaced to the right
with significant increases in the EC50 and significant depressions of the
maximal responses in the presence of the individual agents mibefradil,
indanyloxyacetic acid 94, or nifedipine. A combination of mibefradil and
indanyloxyacetic acid 94 further inhibited the mechanical activity
produced by cirazoline. The further reduction in the maximal response to
cirazoline, in the presence of mibefradil and nifedipine, was
insignificant when compared with the effects of nifedipine alone. In
addition, maximal mechanical responses produced by cirazoline were not
significantly affected by a combination of nifedipine and indanyloxyacetic
acid 94 when compared with either nifedipine alone or mibefradil and
indanyloxyacetic acid 94 combined. Our current findings indicate that
mibefradil, indanyloxyacetic acid 94, and nifedipine can inhibit
cirazoline-induced contractions to a varying degree. Moreover, based on
our present data it would be reasonable to suggest that the contribution
of ***T*** - ***type*** versus L-type Ca2+ channels to contractile
responses obtained with cirazoline are approximately 21% and 35%,
respectively, of the Emax. It would appear that L-type Ca2+ channels play
a greater role in processes that are involved in excitation-contraction
coupling subsequent to stimulation of ***alpha1*** -adrenoceptors. In
addition, Cl- channels also appear to be involved in the process of
contraction following ***alpha1*** -adrenoceptor activation.

L6 ANSWER 10 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:251930 BIOSIS
DOCUMENT NUMBER: PREV200000251930
TITLE: A tale of two (***calcium***) ***channels*** .
AUTHOR(S): Nargeot, Joel (1)
CORPORATE SOURCE: (1) Institut de Genetique Humaine, CNRS UPR 1142, 141 rue
de la Cardonille, 34396, Montpellier cedex, 5 France
SOURCE: Circulation Research, (March 31, 2000) Vol. 86, No. 6, pp.
613-615.
ISSN: 0009-7330.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

L6 ANSWER 11 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)DUPLICATE 2
ACCESSION NUMBER: 2001:11587 SCISEARCH
THE GENUINE ARTICLE: 385NH
TITLE: Structure and regulation of voltage-gated Ca2+ channels
AUTHOR: Catterall W A (Reprint)
CORPORATE SOURCE: Univ Washington, Dept Pharmacol, Box 357280, Seattle, WA
98195 USA (Reprint); Univ Washington, Dept Pharmacol,
Seattle, WA 98195 USA
COUNTRY OF AUTHOR: USA
SOURCE: ANNUAL REVIEW OF CELL AND DEVELOPMENTAL BIOLOGY, (DEC 2000)
Vol. 16, pp. 521-555.
Publisher: ANNUAL REVIEWS, 4139 EL CAMINO WAY, PO BOX
10139, PALO ALTO, CA 94303-0139 USA.
ISSN: 1081-0706.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 218
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Voltage-gated Ca2+ channels mediate Ca2+ entry into cells in response
to membrane depolarization. Electrophysiological studies reveal different
Ca2+ currents designated L-, N-, P-, Q-, R-, and ***T*** - ***type***
. The high-voltage-activated Ca2+ channels that have been characterized
biochemically are complexes of a pore-forming ***alpha*** (***1***
) subunit of similar to 190-250 kDa; a transmembrane, disulfide-linked
complex of alpha (2) and delta subunits; an intracellular beta subunit;
and in some cases a transmembrane gamma subunit. Ten ***alpha*** (
1) subunits, four alpha (2)delta complexes, four beta subunits,
and two gamma subunits are known. The Ca(v)1 family of ***alpha*** (
1) subunits conduct L-type Ca2+ currents, which initiate muscle
contraction, endocrine secretion, and gene transcription, and are
regulated primarily by second messenger-activated protein phosphorylation
pathways. The Ca(v)2 family of ***alpha*** (***1***) subunits
conduct N-type, P/Q-type, and R-type Ca2+ currents, which initiate rapid
synaptic transmission and are regulated primarily by direct interaction
with G proteins and SNARE proteins and secondarily by protein
phosphorylation. The Ca(v)3 family of ***alpha*** (***1***)
subunits conduct ***T*** - ***type*** Ca2+ currents, which are
activated and inactivated more rapidly and at more negative membrane
potentials than other Ca2+ current types. The distinct structures and
patterns of regulation of these three families of Ca2+ channels provide a
flexible array of Ca2+ entry pathways in response to changes in membrane
potential and a range of possibilities for regulation of Ca2+ entry by
second messenger pathways and interacting proteins.

L6 ANSWER 12 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:366087 BIOSIS
DOCUMENT NUMBER: PREV200000366087
TITLE: Analysis of ***T*** - ***type*** ***calcium***
channel function using antisense oligonucleotides.
AUTHOR(S): Feltz, A. (1); Lambert, R. C. (1); Maulet, Y. (1); de
Waard, M.; Perez-Reyes, E.; Volsen, S.
CORPORATE SOURCE: (1) UPR9009-CNRS, Strasbourg France
SOURCE: European Journal of Neuroscience, (2000) Vol. 12, No.
Supplement 11, pp. 317. print.
Meeting Info.: Meeting of the Federation of European
Neuroscience Societies Brighton, UK June 24-28, 2000
ISSN: 0953-816X.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L6 ANSWER 13 OF 104 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000352205 EMBASE
TITLE: Mibefradil block of cloned ***T*** - ***type***
calcium ***channels*** .
AUTHOR: Martin R.L.; Lee J.-H.; Cribbs L.L.; Perez-Reyes E.; Hanck
D.A.
CORPORATE SOURCE: Dr. D.A. Hanck, Cardiology (MC6094), University of Chicago,
5841 South Maryland Ave., Chicago, IL 60637, United States.
d-hanck@uchicago.edu
SOURCE: Journal of Pharmacology and Experimental Therapeutics,
(2000) 295/1 (302-308).
Refs: 34
ISSN: 0022-3565 CODEN: JPETAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Mibefradil is a tetralol derivative chemically distinct from other
calcium ***channel*** antagonists. It is a very effective
antihypertensive agent that is thought to achieve its action via a higher
affinity block for low-voltage-activated (T) than for high-voltage-
activated (L) ***calcium*** ***channels*** . Estimates of affinity
using Ba2+ as the charge carrier have predicted a 10- to 15-fold
preference of mibefradil for T channels over L channels. However, T
channel IC50 values are reported to be .apprx.1 .mu.M, which is much
higher than expected for clinical efficacy because relevant blood levels

of this drug are .apprx.50 nM. We compared the affinity for mibefradil of
the newly cloned T channel isoforms, .alpha.1G, .alpha.1H, and .alpha.1I
with an L channel, .alpha.1C. In 10 mM Ba2+, mibefradil blocked in the
micromolar range and with 12- to 13-fold greater affinity for T channels
than for L channels (.apprx.1 .mu.M versus 13/.mu.M). When 2 mM Ca2+ was
used as the charge carrier, the drug was more efficacious; the IC50 for
.alpha.1G shifted to 270 nM and for . ***alpha*** . ***1*** H shifted
to 140 nM, 4.5- and 9-fold higher affinity than in 10 mM Ba. The data are
consistent with the idea that mibefradil competes for its binding site on
the channel with the permeant species and that Ba2+ is a more effective
competitor than Ca2+. Raising temperature to 35.degree.C reduced affinity
(IC50 792 nM). Reducing channel availability to half increased affinity
(.apprx.70 nM). This profile of mibefradil affinity makes these channels
good candidates for the physiological target of this antihypertensive
agent.

L6 ANSWER 14 OF 104 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000335079 EMBASE
TITLE: Dendro-somatic distribution of calcium-mediated
electrogenesis in Purkinje cells from rat cerebellar slice
cultures.
AUTHOR: Pouille F.; Cavelier P.; Desplantez T.; Beekenkamp H.;
Craig P.J.; Beattie R.E.; Volsen S.G.; Bossu J.L.
CORPORATE SOURCE: J.L. Bossu, Lab. de Neurobiologie Cellulaire, CNRS, Centre
de Neurochimie, 5 rue Blaise Pascal, F-67084 Strasbourg
Cedex, France.
jlbossu@neurochem.u.strasbg.fr
SOURCE: Journal of Physiology, (1 Sep 2000) 527/2 (265-282).
Refs: 51
ISSN: 0022-3751 CODEN: JPHYA7
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
008 Neurology and Neurosurgery
LANGUAGE: English
SUMMARY LANGUAGE: English
AB 1. The role of Ca2+ entry in determining the electrical properties of
cerebellar Purkinje cell (PC) dendrites and somata was investigated in
cerebellar slice cultures. Immunohistofluorescence demonstrated the
presence of at least three distinct types of Ca2+ channel proteins in PCs:
the . ***alpha*** . ***1*** (A) subunit (P/Q type Ca2+ channel), the .
alpha . ***1*** (G) subunit (***T*** ***type***) and the
. ***alpha*** . ***1*** (E) subunit (R type). 2. In PC dendrites, the
response started in 66% of cases with a slow depolarization (50 .+-. 15
ms) triggering one or two fast (.apprx.1 ms) action potentials (APs). The
slow depolarization was identified as a low-threshold non-P/Q Ca2+ AP
initiated, most probably, in the dendrites. In 16% of cases, this response
propagated to the soma to elicit an initial burst of fast APs. 3. Somatic
recordings revealed three modes of discharge. In mode 1, PCs display a
single or a short burst of fast APs. In contrast, PCs fire repetitively in
mode 2 and 3, with a sustained discharge of APs in mode 2, and bursts of
APs in mode 3. Removal of external Ca2+ or bath applications of a
membrane-permeable Ca2+ chelator abolished repetitive firing. 4.
Tetraethylammonium (TEA) prolonged dendritic and somatic fast APs by a
depolarizing plateau sensitive to Cd2+ and to .omega.-agatoxin TK.
Therefore, the role of Ca2+ channels in determining somatic PC firing has
been investigated. Cd2+ or P/Q type Ca2+ channel-specific toxins reduced
the duration of the discharge and occasionally induced the appearance of
oscillations in the membrane potential associated with bursts of APs. 5.
In summary, we demonstrate that Ca2+ entry through low-voltage gated Ca2+
channels, not yet identified, underlies a dendritic AP rarely eliciting a
somatic burst of APs whereas Ca2+ entry through P/Q type Ca2+ channels
allowed a repetitive firing mainly by inducing a Ca2+-dependent
hyperpolarization.

L6 ANSWER 15 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:621150 SCISEARCH
THE GENUINE ARTICLE: 343GL
TITLE: Molecular diversity of voltage-gated ***calcium***
channels
AUTHOR: Lory P; Monteil A; Chemin J; Leuranguer V; Bourinet E;
Nargeot J (Reprint)
CORPORATE SOURCE: CNRS, UPR 1142, IGH, PHYSIOPATHOL CANAUX ION, 14 RUE
CARDONILLE, F-34396
MONTPELLIER 05, FRANCE (Reprint);
CNRS, UPR 1142, IGH, PHYSIOPATHOL CANAUX ION, F-34396
MONTPELLIER 05, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: THERAPIE, (MAR-APR 2000) Vol. 55, No. 2, pp. 249-254.
Publisher: JOHN LIBBEY & CO LTD, 13 SMITHS YARD, SUMMERLEY
ST, LONDON SW18 4HR, ENGLAND.
ISSN: 0040-5957.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: French
REFERENCE COUNT: 16
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Voltage-gated ***calcium*** ***channels*** are involved in a
large variety of cellular functions such as excitation-contraction
coupling, hormone secretion. firing and pacemaker activity, gene
activation and proliferation. Cloning of complementary DNAs encoding for
calcium ***channel*** subunits has challenged the study of the
functional properties of ***calcium*** ***channels*** and has
allowed analysis of the molecular basis of ***calcium***
channel diversity. Recently, pore-forming subunits of ***T*** -
type ***calcium*** ***channels*** have been cloned. Recent
data describing type genes encoding ***calcium*** ***channels*** ,
their molecular and pharmacological studies, as well as their linkage to
human genetic diseases are reviewed in this article.

L6 ANSWER 16 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:525133 BIOSIS
DOCUMENT NUMBER: PREV200000525133
TITLE: Modulation of the deactivation kinetics of a recombinant
rat ***T*** - ***type*** Ca2+ channel by prior
inactivation.
AUTHOR(S): Warre, Ruth; Randall, Andrew (1)
CORPORATE SOURCE: (1) Neuroscience Research, SmithKline Beecham
Pharmaceuticals, New Frontiers Science Park, North Harlow,
Essex UK
SOURCE: Neuroscience Letters, (November 3, 2000) Vol. 293, No. 3,
pp. 216-220. print.
ISSN: 0304-3940.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Using patch clamp methods we have investigated the deactivation properties
of the ***T*** - ***type*** Ca2+ channel generated by expression of
the rat alpha1I subunit in HEK293 cells. The amplitude of the
repolarisation-induced tail current was strongly correlated (R = 0.998)
with the current amplitude immediately prior to repolarisation. The rate
of deactivation was voltage-dependent between -120 mV (taudeact = 0.9 +-
0.0 ms) and -60 mV (taudeac = 3.3 +- 0.5 ms). Interestingly, the rate of
deactivation observed at -80 mV was clearly dependent on the level of
inactivation induced immediately prior to repolarisation, with greater
inactivation producing significantly slower deactivation. In contrast, the
rate of deactivation appeared completely independent of the level of
steady-state inactivation. Together these data indicate the presence of a
tight relationship between the recent induction of inactivation of this
T - ***type*** channel and its subsequent rate of deactivation.

L6 ANSWER 17 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:180035 BIOSIS
DOCUMENT NUMBER: PREV200000180035
TITLE: Identification of multiple human alpha1G isoforms of
T - ***type*** ***calcium*** ***channels***
with distinct functional properties.
AUTHOR(S): Monteil, Arnaud (1); Chemin, Jean (1); Bourinet, Emmanuel
(1); Nargeot, Joel (1); Lory, Philippe (1)
CORPORATE SOURCE: (1) CNRS, IGH, 34396, Montpellier France
SOURCE: Biophysical Journal, (Jan., 2000) Vol. 78, No. 1 Part 2,
pp. 199A.
Meeting Info.: 44th Annual Meeting of the Biophysical
Society. New Orleans, Louisiana, USA February 12-16, 2000
ISSN: 0006-3495.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L6 ANSWER 18 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2001:67602 SCISEARCH
THE GENUINE ARTICLE: 389BX
TITLE: Modulation of recombinant ***T*** - ***type*** Ca2+
channels by hypoxia and glutathione
AUTHOR: Fearon I M (Reprint); Randall A D; Perez-Reyes E; Peers C
CORPORATE SOURCE: Univ Leeds, Inst Cardiovasc Res, Leeds LS2 9JT, W
Yorkshire, England (Reprint); SmithKline Beecham
Pharmaceut, Dept Neurosci Res, Harlow CM19 5AW, Essex,
England; Univ Virginia, Dept Pharmacol, Charlottesville,
VA 22908 USA
COUNTRY OF AUTHOR: England; USA
SOURCE: PFLUGERS ARCHIV-EUROPEAN JOURNAL OF

PHYSIOLOGY, (DEC 2000)
Vol. 441, No. 2-3, pp. 181-188.
Publisher: SPRINGER-VERLAG, 175 FIFTH AVE, NEW YORK, NY
10010 USA.
ISSN: 0031-6768.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 37
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB ***T*** - ***type*** Ca2+ channels are expressed in a wide
variety of central and peripheral neurons and play an important role in
neuronal firing and rhythmicity. Here we examined the effects of hypoxia
on the recently cloned ***T*** - ***type*** Ca2+ channel alpha (1G),
alpha (1H) and alpha (11) subunits, stably expressed in HEK 293 cells. In
cells expressing the human alpha (1H) or the rat alpha (11) subunit, Ca2+
channel currents were inhibited reversibly by hypoxia (PO2<110 mmHg). The
degree of inhibition was more marked in cells expressing the <alpha>(1H)
subunit. This hypoxic inhibition was not voltage dependent. In cells
expressing the rat alpha (1G) subunit, hypoxia caused no detectable
reduction in Ca2+ channel activity. Regardless of the channel type
examined, hypoxia was without effect on the kinetic properties of the Ca2+
current (activation, inactivation and deactivation) or on steady-state
inactivation. Ca2+ current through the alpha (1H) subunit was enhanced by
the reducing agent reduced glutathione (GSH; 2 mM) and inhibited by
oxidised glutathione (GSSG; 2 mM). In contrast, Ca2+ current through the
alpha (1G) subunit was unaffected by GSH. In alpha (1H) cells, neither GSH
nor GSSG had any effect on the ability of hypoxia to reduce Ca2+ current
amplitudes. Thus, different members of the ***T*** - ***type*** Ca2+
channel family are differently regulated by hypoxia and redox agents.
Hypoxic regulation of the alpha (1H) subunit appears to be independent of
changes in levels of the intracellular redox couple GSSG:GSH.

L6 ANSWER 19 OF 104 MEDLINE
DUPLICATE 3
ACCESSION NUMBER: 2000412064 MEDLINE
DOCUMENT NUMBER: 20382745
TITLE: Overexpression of ***T*** - ***type***
calcium ***channels*** in HEK-293 cells
increases intracellular calcium without affecting cellular
proliferation.
AUTHOR: Chemin J; Monteil A; Briquaire C; Richard S; Perez-Reyes E;
Nargeot J; Lory P
CORPORATE SOURCE: IGH-CNRS UPR 1142-141, rue de la Cardonille, F-34396
Montpellier, Cedex 05, France.
SOURCE: FEBS LETTERS, (2000 Jul 28) 478 (1-2) 166-72.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY WEEK: 20001101
AB Increased expression of low voltage-activated, ***T*** - ***type***
Ca(2+) channels has been correlated with a variety of cellular events
including cell proliferation and cell cycle kinetics. The recent cloning
of three genes encoding ***T*** - ***type*** ***alpha*** (***1***) subunits, alpha(1G), alpha(1H) and alpha(1I), now allows direct
assessment of their involvement in mediating cellular proliferation. By
overexpressing the human alpha(1G) and alpha(1H) subunits in human
embryonic kidney (HEK-293) cells, we describe here that, although
T - ***type*** channels mediate increases in intracellular
Ca(2+) concentrations, there is no significant change in bromodeoxyuridine
incorporation and flow cytometric analysis. These results demonstrate that
expressions of ***T*** - ***type*** Ca(2+) channels are not
sufficient to modulate cellular proliferation of HEK-293 cells.

L6 ANSWER 20 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:66866 SCISEARCH
THE GENUINE ARTICLE: 275HL
TITLE: Expression of mRNAs for the ***alpha*** (***1***)
subunit of voltage-gated ***calcium*** ***channels*** in human osteoblast-like cell lines and
in normal human osteoblasts
AUTHOR: Barry E L R (Reprint)
CORPORATE SOURCE: DARTMOUTH COLL SCH MED, DEPT PHARMACOL & TOXICOL, HANOVER,
NH 03755 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: CALCIFIED TISSUE INTERNATIONAL, (FEB 2000) Vol. 66, No. 2,
pp. 145-150.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY
10010.
ISSN: 0171-967X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 37
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The activation of osteoblast ***calcium*** ***channels*** by
many bone regulatory factors suggests an important role for intracellular
calcium signaling in the control of bone remodeling. At least six
different genes for the ***alpha*** (***1***) subunit of
voltage-gated ***calcium*** ***channels*** have been cloned
including L-type (alpha(1S), alpha(1C) and alpha(1D)) and non-L-type
(alpha(1A), alpha(1B), and alpha(1E)) isoforms. The goal of the present
study was to identify which of these ***calcium*** ***channel***
isoforms are transcribed in human osteoblast-like cell lines (hFOB, MG-63,
SAOS-2, TE-85, G-292) and in cultures of normal human osteoblasts. Reverse
transcriptase-PCR was used to amplify sequences corresponding to each of
the ***alpha*** (***1***) subunits using isoform specific primers.
The products of the PCR reaction were cloned and sequenced to verify their
identity and used to probe southern blots of the PCR reactions. The
results indicate that among the different types of osteoblast-like cells
examined, two ***calcium*** ***channel*** isoforms were always
expressed (alpha(1C) and alpha(1A)), three isoforms were variably
expressed (alpha(1S), alpha(1D) and alpha(1B)), and one isoform was not
expressed in any of the osteoblast-like cells (alpha(1E)) but was easily
detected in human brain controls. Our results indicate that mRNAs for
multiple ***calcium*** ***channel*** ***alpha*** (***1***)
subunits are expressed in human osteoblasts, including both L-type and
non-L-type isoforms. In addition, significant heterogeneity exists between
the different osteoblast cell models examined in the type and mRNA
abundance of the different ***calcium*** ***channel*** isoforms.

L6 ANSWER 21 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:777453 SCISEARCH
THE GENUINE ARTICLE: 362PP
TITLE: Low voltage activated ***calcium*** ***channels***
: from genes to function
AUTHOR: Lacinova L (Reprint); Klugbauer N; Hofmann F
CORPORATE SOURCE: TECH UNIV MUNICH, INST PHARMAKOL & TOXIKOL, BIEDERSTEINER
STR 29, D-80802 MUNICH, GERMANY (Reprint); SLOVAK ACAD
SCI, INST MOL PHYSIOL & GENET, BRATISLAVA 83304, SLOVAKIA
COUNTRY OF AUTHOR: GERMANY; SLOVAKIA
SOURCE: GENERAL PHYSIOLOGY AND BIOPHYSICS, (JUN 2000) Vol. 19, No.
2, pp. 121-136.
Publisher: GENERAL PHYSIOL AND BIOPHYSICS, INST OF MOLEC
PHYSIOL GENETICS SLOVAK ACAD OF SCI VLARSKA 5, 83334
BRATISLAVA, SLOVAKIA.
ISSN: 0231-5882.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 44
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Cloning of three members of low-voltage-activated (LVA) ***calcium*** ***channel*** family, predominantly neuronal alpha(1G) and alpha(1I),
and ubiquitous alpha(1H), enabled to investigate directly their
electrophysiological and pharmacological profile as well as their putative
subunit composition. All the three channels are half-activated at membrane
potential about -40 mV and half-inactivated at about -70 mV. Kinetics of
alpha(1G) and alpha(1H) channels activation and inactivation are similar
and faster than that of alpha(1I) channel. All the three channels are
blocked with high affinity by the organic blocker mibefradil. Another high
affinity blocker is kurtoxin. Cloned LVA channels are relatively
insensitive to antiepileptics, dihydropyridines and w-conotoxins. Ni2+ is
high affinity blocker of alpha(1H) channel only. Amiloride inhibits the
alpha(1H) channel.
The subunit composition of LVA channel remains unclear. Cut of known
high-voltage-activated ***calcium*** ***channel*** subunits,
alpha(2)delta-2 and gamma-5 subunits significantly and systematically
modified activation and/or inactivation of the current. In contrast,
alpha(2)delta-1, alpha(2)delta-3, gamma-2 and gamma-4 subunits failed to
modulate the current or had only minor effects.

L6 ANSWER 22 OF 104 MEDLINE
DUPLICATE 4
ACCESSION NUMBER: 2000081696 MEDLINE
DOCUMENT NUMBER: 20081696
TITLE: Cloning of a ***T*** - ***type*** Ca2+ channel
isoform in insulin-secreting cells.

AUTHOR: Zhuang H; Bhattacharjee A; Hu F; Zhang M; Goswami T; Wang
L; Wu S; Berggren P O; Li M
CORPORATE SOURCE: Department of Pharmacology, College of Medicine, University
of South Alabama, Mobile 36688, USA.
CONTRACT NUMBER: DK-05151 (NIDDK)
SOURCE: DIABETES, (2000 Jan) 49 (1) 59-64.
Journal code: E8X. ISSN: 0012-1797.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
OTHER SOURCE: GENBANK-AF125161
ENTRY MONTH: 200003
ENTRY WEEK: 20000304
AB The ***T*** - ***type*** Ca2+ channel is an important determinant of
electrical activity and of Ca2+ influx in rat and human pancreatic
beta-cells. We have identified and sequenced a cDNA encoding a ***T***
- ***type*** Ca2+ channel ***alpha1*** -subunit derived from INS-1,
the rat insulin-secreting cell line. The sequence of the cDNA indicates a
protein composed of 2,288 amino acids that shares 96.3% identity to
alpha1G, the neuronal ***T*** - ***type*** Ca2+ channel subunit. The
transmembrane domains of the protein are highly conserved, but the isoform
contains three distinct regions and 10 single amino acid substitutions in
other regions. Sequencing rat genomic DNA revealed that the ***alpha1***
-subunit we cloned is an alternative splice isoform of alpha1G. By using
specific primers and reverse transcription-polymerase chain reaction, we
demonstrated that both splice variants are expressed in rat islets. The
isoform deduced from INS-1 was also expressed in brain, neonatal heart,
and kidney. Functional expression of this alpha1G isoform in Xenopus
oocytes generated low voltage-activated Ba2+ currents. These results
provide the molecular biological basis for studies of function of
T - ***type*** Ca2+ channels in beta-cells, which is where these
channels may play critical roles in diabetes.

L6 ANSWER 23 OF 104 MEDLINE
DUPLICATE 5
ACCESSION NUMBER: 2000127580 MEDLINE
DOCUMENT NUMBER: 20127580
TITLE: Determinants of voltage-dependent inactivation affect
Mibefradil block of ***calcium*** ***channels*** .
AUTHOR: Jimenez C; Bourinet E; Leuranguer V; Richard S; Snutch T P;
Nargeot J
CORPORATE SOURCE: Institut de Genetique Humaine, CNRS UPR1142, Montpellier,
France.
SOURCE: NEUROPHARMACOLOGY, (2000) 39 (1) 1-10.
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000404
AB The voltage gated ***calcium*** ***channel*** family is a major
target for a range of therapeutic drugs. Mibefradil (Ro 40-5967) belongs
to a new chemical class of these molecules which differs from other Ca2+
antagonists by its ability to potently block ***T*** - ***type***
Ca2+ channels. However, this molecule has also been shown to inhibit other
Ca2+ channel subtypes. To further analyze the mechanism governing the Ca2+
channel-Mibefradil interaction, we examined the effect of Mibefradil on
various recombinant Ca2+ channels expressed in mammalian cells from their
cloned cDNAs, using Ca2+ as the permeant ion at physiological
concentration. Expression of alpha1A, alpha1C, and alpha1E in tsA 201
cells resulted in Ca2+ currents with functional characteristics closely
related to those of their native counterparts. Mibefradil blocked alpha1A
and alpha1E with a Kd comparable to that reported for ***T*** -
type channels, but had a lower affinity (approximately 30-fold)
for alpha1C. For each channel, inhibition by Mibefradil was consistent
with high-affinity binding to the inactivated state. Modulation of the
voltage-dependent inactivation properties by the nature of the coexpressed
beta subunit or the ***alpha1*** splice variant altered block at the
Mibefradil receptor site. Therefore, we conclude that the tissue and
sub-cellular localization of ***calcium*** ***channel*** subunits
as well as their specific associations are essential parameters to
understand the in vivo effects of Mibefradil.

L6 ANSWER 24 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:82581 BIOSIS
DOCUMENT NUMBER: PREV200100082581
TITLE: Modulation of alpha1G and alpha1C Ca channels by the spider
toxin ProTx-II.
AUTHOR(S): Kraus, R. L. (1); Warren, V. A.; Smith, M. M.; Middleton,
R. E.; Cohen, C. J.
CORPORATE SOURCE: (1) Merck Research Labs, Rahway, NJ USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No.
1-2, pp. Abstract No.-234.14. print.
Meeting Info.: 30th Annual Meeting of the Society of
Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Toxin-II from the venom of Prosphapalopus anomalous (ProTx-II) was
isolated based on its ability to inhibit PN1 and PN3 Na channels expressed
in Xenopus oocytes. The toxin has 6 cysteines that conform to the
inhibitory cystine knot (ICK) motif found in hanatoxin (a K channel
inhibitor) and omega-grammotoxin-SIA (an inhibitor of N- and P-type Ca
channels). We studied inhibition of PN1 Na channels and alpha1G (***T***
- ***type***) and alpha1C (L-type) Ca channels expressed in HEK cells.
For alpha1G Ca channels, 1 muM ProTX-II shifts current activation apprx 35
mV to more positive voltages and reduces the steepness of voltage
dependence of activation. The toxin slows activation even during strong
depolarizations and speeds deactivation upon repolarization. Block of
current during weak depolarizations indicates an apparent IC50 simeq100
nM. Although ProTx-II inhibits channel opening, it does not alter
steady-state inactivation, indicating that channels can inactivate from
closed states. ProTx-II inhibits alpha1C Ca channels and PN1 Na channels
with comparable potency as for alpha1G Ca channels and with similar
effects on channel activation. Thus, ProTx-II has an ICK motif also found
in hanatoxin and omega-grammotoxin-SIA and it modifies channel gating in
an analogous manner to these toxins. This suggests that ProTx- II does not
simply occlude the pore of Na and Ca channels and instead inhibits channel
activation by binding to an extracellular S3-S4 linker. ProTx-II
identifies a functional domain conserved among Ca and Na channels that is
important for channel activation.

L6 ANSWER 25 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2001:76219 BIOSIS
DOCUMENT NUMBER: PREV200100076219
TITLE: Cloning, distribution, and functional expression of a human
alpha1I low voltage-activated Ca channel.
AUTHOR(S): Gomora, J. C. (1); Daud, A.; McNaughton, N. C.; Medhurst,
A.; Green, P.; Pangalos, M. N.; Randall, A. D.;
Perez-Reyes, E.
CORPORATE SOURCE: (1) University of Virginia, Charlottesville, VA USA
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26, No.
1-2, pp. Abstract No.-135.11. print.
Meeting Info.: 30th Annual Meeting of the Society of
Neuroscience New Orleans, LA, USA November 04-09, 2000
Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English
AB In silico cloning led to the identification of three genes that encode
alpha1 subunits of ***T*** - ***type*** Ca2+ channels:
alpha1G (Cav3.1), alpha1H (Cav3.2), and alpha1I (Cav3.3). The alpha1I
subunit was discovered while cloning from a rat brain cDNA library (Lee et
al., J. Neurosci. 19:1912, 1999). Here we report the cloning of the human
ortholog of alpha1I. Fetal brain and adult cerebellum libraries were
screened at low stringency using cDNA probes derived from rat alpha1I. The
deduced amino acid sequence is 93% identical to the rat alpha1I. The human
clone has a much longer carboxyl terminus. The divergence occurs at an
intron/exon boundary, with the rat cDNA being spliced in a different frame
that terminates shortly thereafter. BLAST searches identified a partial
clone (GenBank AB032946) that encoded the full carboxyl terminus and 3.3
kb of the 3' untranslated sequence. The distribution of alpha1I mRNA was
studied using PCR amplification with Taqman, and normalized to
cyclophilin. The gene is almost exclusively expressed in the brain, with
high expression in cerebral cortex, basal ganglia, hippocampus, and
amygdala. Expression of the channel in HEK-293 cells led to the induction
of typical ***T*** - ***type*** currents, with the notable exception
that they activated and inactivated much more slowly.

L6 ANSWER 26 OF 104 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
DUPLICATE 6
ACCESSION NUMBER: 1999-371096 [31] WPIDS
DOC. NO. CPI: C1999-109562
TITLE: Subunits of ***calcium*** ***channels*** .
DERWENT CLASS: B04 D16

INVENTOR(S): HANS, M; HARPOLD, M; STAUDERMAN, K; URRUTIA, A; WASHBURN, M S; WILLIAMS, M
PATENT ASSIGNEE(S): (SIBI-N) SIBIA NEUROSCIENCES INC; (MERI) MERCK & CO INC
COUNTRY COUNT: 84
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9928342	A2	19990610 (199931)*		EN	169

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9918026 A 19990616 (199945)
EP 1042468 A2 20001011 (200052) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MK NL PT RO SE SI

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION DATE
WO 9928342	A2	WO 1998-US25671 19981203
AU 9918026	A	AU 1999-18026 19981203
EP 1042468	A2	EP 1998-962884 19981203
		WO 1998-US25671 19981203

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9918026	A Based on	WO 9928342
EP 1042468	A2 Based on	WO 9928342

PRIORITY APPLN. INFO: US 1998-188932 19981110; US 1997-984709 19971203
AN 1999-371096 [31] WPIDS
AB WO 9928342 A UPAB: 19990806
NOVELTY - An isolated nucleic acid fragment (I) that encodes a low-voltage activated subunit of an animal ***calcium*** ***channel*** .
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:
(1) a eukaryotic cell, comprising heterologous nucleic acid that encodes an ***alpha*** ***1*** subunit wherein the ***alpha*** ***1*** subunit is encoded by (I);
(2) a eukaryotic cell with a functional, heterologous ***calcium*** ***channel*** , produced by a process comprising introducing into the cell heterologous nucleic acid that encodes at least one subunit of a ***calcium*** ***channel*** , wherein the subunit is encoded by (I);
(3) a method for identifying a compound that modulates the activity of a ***calcium*** ***channel*** that contains an ***alpha*** ***1*** subunit, comprising;
(a) suspending the eukaryotic cell of any as in (1) or (2) in a solution containing the compound and a ***calcium*** ***channel*** selective ion;
(b) depolarizing the cell membrane of the cell; and
(c) detecting the current or ions flowing into the cell, where:
(i) the heterologous ***calcium*** ***channel*** includes at least one ***calcium*** ***channel*** subunit encoded by DNA or RNA that is heterologous to the cell;
(ii) the current that is detected is different from that produced by depolarizing the same or a substantially identical cell in the presence of the same ***calcium*** ***channel*** selective ion but in the absence of the compound;
(4) a ***alpha*** ***1*** -subunit encoded by the nucleic acid molecule (I);
(5) an RNA or DNA probe of at least 16 bases in length, comprising at least 16 contiguous nucleic acid bases from (I) that encode an alpha 1H-subunit of a ***calcium*** ***channel*** ;
(6) a eukaryotic cell, comprising a heterologous ***calcium*** ***channel*** encoded by nucleic acid encoding an ***alpha*** ***1*** -subunit of a ***calcium*** ***channel*** , wherein the heterologous ***calcium*** ***channel*** is a low voltage activated channel or a ***T*** - ***type*** channel;
(7) an isolated nucleic acid molecule, comprising nucleotides 1506 to 2627 of the 7898 bp sequence given in the specification;
(8) a method for identifying compounds that modulate the activity of a low-voltage activated ***calcium*** ***channel*** ;
(9) a screening assay for identifying a compound that modulates the activity of a low-voltage activated (LVA) ***calcium*** ***channel*** ;
(10) a compound identified by the method as in (8) or (9).
(11) a method of identifying compounds for treatment of low-voltage activated (LVA) type ***calcium*** ***channel*** mediated disorders, comprising identifying compounds that modulate the activity of LVA-type channels in cells that express channels containing a subunit encoded by the nucleic acid (I).
ACTIVITY - None given.
MECHANISM OF ACTION - None given.
USE - The probes can be used to identify nucleic acids that encode an alpha 1H subunit of a ***calcium*** ***channel*** subunit. The probes can also be used to identify cells or tissues that express this subunit. The method as in (11) ma be used to detect neurological, endocrinological, cardiovascular, urological, hepatic, respiratory, and vascular disorders. (All claimed)
Dwg.0/4

L6 ANSWER 27 OF 104 MEDLINE
ACCESSION NUMBER: 1999357772 MEDLINE
DOCUMENT NUMBER: 99357772
TITLE: Multiple structural domains contribute to voltage-dependent inactivation of rat brain alpha(1E) ***calcium*** ***channels*** .
AUTHOR: Spaetgens R L; Zamponi G W
CORPORATE SOURCE: Department of Pharmacology and Therapeutics, Neuroscience Research Group, University of Calgary, Calgary, Alberta T2N 4N1, Canada.
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1999 Aug 6) 274 (32) 22428-36.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199911
AB We have investigated the molecular determinants that mediate the differences in voltage-dependent inactivation properties between rapidly inactivating (R-type) alpha(1E) and noninactivating (L-type) alpha(1C) ***calcium*** ***channels*** . When coexpressed in human embryonic kidney cells with ancillary beta(1b) and alpha(2)-delta subunits, the wild type channels exhibit dramatically different inactivation properties; the half-inactivation potential of alpha(1E) is 45 mV more negative than that observed with alpha(1C), and during a 150-ms test depolarization, alpha(1E) undergoes 65% inactivation compared with only about 15% for alpha(1C). To define the structural determinants that govern these intrinsic differences, we have created a series of chimeric ***calcium*** ***channel*** ***alpha*** (***1***) subunits that combine the major structural domains of the two wild type channels, and we investigated their voltage-dependent inactivation properties. Each of the four transmembrane domains significantly affected the half-inactivation potential, with domains II and III being most critical. In particular, substitution of alpha(1C) sequence in domains II or III with that of alpha(1E) resulted in 25-mV negative shifts in half-inactivation potential. Similarly, the differences in inactivation rate were predominantly governed by transmembrane domains II and III and to some extent by domain IV. Thus, voltage-dependent inactivation of alpha(1E) channels is a complex process that involves multiple structural domains and possibly a global conformational change in the channel protein.

L6 ANSWER 28 OF 104 MEDLINE
DUPLICATE 7
ACCESSION NUMBER: 2000062483 MEDLINE
DOCUMENT NUMBER: 20062483
TITLE: Comparison of the Ca2 + currents induced by expression of three cloned ***alpha1*** subunits, alpha1G, alpha1H and alpha1I, of low-voltage-activated ***T*** - ***type*** Ca2 + channels.
AUTHOR: Klockner U; Lee J H; Cribbs L L; Daud A; Hescheler J; Pereverzev A; Perez-Reyes E; Schneider T
CORPORATE SOURCE: Institute of Vegetative Physiology, University of Cologne, Koln, Germany.
CONTRACT NUMBER: HL58728 (NHLBI)
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (1999 Dec) 11 (12) 4171-8.
Journal code: BYG. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000402
AB Expression of rat alpha1G, human alpha1H and rat alpha1I subunits of voltage-activated Ca2 + channels in HEK-293 cells yields robust Ca2 + inward currents with 1.25 mM Ca2 + as the charge carrier. Both similarities and marked differences are found between their biophysical properties. Currents induced by expression of alpha1G show the fastest activation and inactivation kinetics. The alpha1H and

alpha1I currents
activate and inactivate up to 1.5- and 5-fold slower, respectively. No
differences in the voltage dependence of steady state inactivation are
detected. Currents induced by expression of alpha1G and alpha1H deactivate
with time constants of up to 6 ms at a test potential of - 80 mV, but
currents induced by alpha1I deactivate about three-fold faster. Recovery
from short-term inactivation is more than three-fold slower for currents
induced by alpha1H and alpha1I in comparison to alpha1G. In contrast to
these characteristics, reactivation after long-term inactivation was
fastest for currents arising from expression of alpha1I and slowest in
cells expressing alpha1H ***calcium*** ***channels*** . The calcium
inward current induced by expression of alpha1I is increased by positive
prepulses while currents induced by alpha1H and alpha1G show little (<
5%) or no facilitation. The data thus provide a characteristic fingerprint
of each channel's activity, which may allow correlation of the alpha1G,
alpha1H and alpha1I induced currents with their in vivo counterparts.

L6 ANSWER 29 OF 104 MEDLINE
DUPLICATE 8
ACCESSION NUMBER: 2000062481 MEDLINE
DOCUMENT NUMBER: 20062481
TITLE: Distinct kinetics of cloned ***T*** - ***type*** Ca2
+ channels lead to differential Ca2 + entry and
frequency-dependence during mock action potentials.
AUTHOR: Kozlov A S; McKenna F; Lee J H; Cribbs L L; Perez-Reyes E;
Feltz A; Lambert R C
CORPORATE SOURCE: Laboratoire de Neurobiologie Cellulaire; UPR 9009-CNRS,
Strasbourg, France.
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (1999 Dec) 11 (12)
4149-58.
Journal code: BYG. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY WEEK: 20000402
AB Voltage-dependent activity around the resting potential is determinant in
neuronal physiology and participates in the definition of the firing
pattern. Low-voltage-activated ***T*** - ***type*** Ca2 + channels
directly affect the membrane potential and control a number of secondary
Ca2 + -dependent permeabilities. We have studied the ability of the cloned
T - ***type*** channels (alpha1G,H,I) to carry Ca2 + currents in
response to mock action potentials. The relationship between the spike
duration and the current amplitude is specific for each of the ***T***
- ***type*** channels, reflecting their individual kinetic properties.
Typically the charge transfer increases with spike broadening, but the
total Ca2 + entry saturates at different spike durations according to the
channel type: 4 ms for alpha1G; 7 ms for alpha1H; and > 10 ms for alpha1I
channels. During bursts, currents are inhibited and/or transiently
potentiated according to the ***alpha1*** channel type, with larger
effects at higher frequency. The inhibition may be induced by
voltage-independent transitions toward inactivated states and/or channel
inactivation through intermediate closed states. The potentiation is
explained by an acceleration in the channel activation kinetics.
Relatively fast inactivation and slow recovery limit the ability of
alpha1G and alpha1H channels to respond to high frequency stimulation (>
20 Hz). In contrast, the slow inactivation of alpha1I subunits allows
these channels to continue participating in high frequency bursts (100
Hz). The biophysical properties of alpha1G, H and I channels will
therefore dramatically modulate the effect of neuronal activities on Ca2 +
signalling.

L6 ANSWER 30 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:61227 BIOSIS
DOCUMENT NUMBER: PREV200000061227
TITLE: Nickel block of three cloned ***T*** - ***type*** ***calcium*** ***channels*** : Low concentrations
selectively block alpha1H.
AUTHOR(S): Lee, Jung-Ha; Gomora, Juan Carlos; Cribbs, Leanne L.;
Perez-Reyes, Edward (1)
CORPORATE SOURCE: (1) Department of Pharmacology, University of Virginia,
1300 Jefferson Park Avenue, Charlottesville, VA USA
SOURCE: Biophysical Journal, (Dec., 1999) Vol. 77, No. 6, pp.
3034-3042.
ISSN: 0006-3495.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Nickel has been proposed to be a selective blocker of low-voltage-
activated, ***T*** - ***type*** ***calcium*** ***channels***
. However, studies on cloned high-voltage-activated Ca2+ channels
indicated that some subtypes, such as alpha1E, are also blocked by low
micromolar concentrations of NiCl2. There are considerable differences in
the sensitivity to Ni2+ among native ***T*** - ***type*** currents,
leading to the hypothesis that there may be more than one ***T*** -
type channel. We confirmed part of this hypothesis by cloning
three novel Ca2+ channels, alpha1G, H, and I, whose currents are nearly
identical to the biophysical properties of native ***T*** - ***type***
channels. In this study we examined the nickel block of these cloned
T - ***type*** channels expressed in both Xenopus oocytes and
HEK-293 cells (10 mM Ba2+). Only alpha1H currents were sensitive to low
micromolar concentrations (IC50 = 13 muM). Much higher concentrations were
required to half-block alpha1I (216 muM) and alpha1G currents (250 muM).
Nickel block varied with the test potential, with less block at potentials
above -30 mV. Outward currents through the T channels were blocked even
less. We show that depolarizations can unblock the channel and that this
can occur in the absence of permeating ions. We conclude that Ni2+ is only
a selective blocker of alpha1H currents and that the concentrations
required to block alpha1G and alpha1I will also affect
high-voltage-activated calcium currents.

L6 ANSWER 31 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:653424
SCISEARCH
THE GENUINE ARTICLE: 226UZ
TITLE: Distribution of the voltage-dependent ***calcium***
channel alpha(1G) subunit mRNA and protein
throughout the mature rat brain
AUTHOR: Craig P J (Reprint); Beattie R E; Folly E A; Banerjee M D;
Reeves M B; Priestley J V; Carney S L; Sher E; PerezReyes
E; Volsen S G
CORPORATE SOURCE: ELI LILLY & CO, LILLY RES CTR LTD, ERL WOOD MANOR,
WINDLESHAM GU20 6PH, SURREY, ENGLAND (Reprint); ST
BARTHOLOMEWS, DIV BIOMED SCI, NEUROSCI SECT, LONDON E1
4NS, ENGLAND; UNIV LONDON QUEEN MARY & WESTFIELD COLL,
ROYAL LONDON SCH MED & DENT, LONDON E1 4NS, ENGLAND;
LOYOLA UNIV, MED CTR, DEPT PHYSIOL, MAYWOOD, IL 60153
COUNTRY OF AUTHOR: ENGLAND; USA
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (AUG 1999) Vol. 11, No.
8, pp. 2949-2964.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD,
OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0953-816X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 56
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The molecular identity of a gene which encodes the pore-forming subunit
(alpha(1G)) of a member of the family of low-voltage-activated, ***T***
- ***type*** , voltage-dependent ***calcium*** ***channels***
has been described recently. Although northern mRNA analyses have shown
alpha(1G) to be expressed predominantly in the brain, the detailed
cellular distribution of this protein in the central nervous system (CNS)
has not yet been reported. The current study describes the preparation of
a subunit specific alpha(1G) riboprobe and antiserum which have been used
in parallel in situ mRNA hybridization and immunohistochemical studies to
localize alpha(1G) in the mature rat brain. Both alpha(1G) mRNA and
protein were widely distributed throughout the brain, but variations were
observed in the relative level of expression in discrete nuclei.
Immunoreactivity for alpha(1G) was typically localized in both the soma
and dendrites of many neurons. Whilst alpha(1G) protein and mRNA
expression were often observed in cells known to exhibit ***T*** -
type current activity, some was also noted in regions, e.g.
cerebellar granule cells, in which ***T*** - ***type*** activity has
not been described. These observations may reflect differences between the
subcellular distribution of channels that can be identified by
immunohistochemical methods compared with electrophysiological techniques.

L6 ANSWER 32 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:410324
SCISEARCH
THE GENUINE ARTICLE: 198YU
TITLE: Excitatory but not inhibitory synaptic transmission is
reduced in lethargic(Cacnb4(1h)) and tottering

(Cacnala(tg)) mouse thalami
AUTHOR: Caddick S J; Wang C S; Fletcher C F; Jenkins N A; Copeland
N G; Hosford D A (Reprint)
CORPORATE SOURCE: DUKE UNIV, DEPT MED NEUROL, BLDG 16, RM 38, 508 FULTON ST,
DURHAM, NC 27705 (Reprint); DUKE UNIV, DEPT MED NEUROL,
DURHAM, NC 27705; VET ADM MED CTR, DURHAM, NC 27705;
VIRGINIA COMMONWEALTH UNIV, MED COLL VIRGINIA, DEPT
NEUROL, RICHMOND, VA 23298; DUKE UNIV, MED CTR, DEPT MED,
DIV NEUROL, DURHAM, NC 27705; DUKE UNIV, MED CTR, DEPT
NEUROBIOL, DURHAM, NC 27705; NCI, MAMMALIAN GENET LAB, ADV
BIOSCI LABS, BASIC RES PROGRAM, FREDERICK CANC RES & DEV
CTR, FREDERICK, MD 21702
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF NEUROPHYSIOLOGY, (MAY 1999) Vol. 81, No. 5, pp.
2066-2074.
Publisher: AMER PHYSIOLOGICAL SOC, 9650 ROCKVILLE PIKE,
BETHESDA, MD 20814.
ISSN: 0022-3077.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 58
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Recent studies of the homozygous tottering (Cacnala(tg)) and lethargic
mouse (Cacnb4(lh)) models of absence seizures have identified mutations in
the genes encoding the alpha 1A and beta 4 subunits, respectively, of
voltage-gated Ca2+ channels (VGCCs). beta subunits normally regulate Ca2+
currents via a direct interaction with ***alpha*** ***1***
(pore-forming) subunits of VGCCs, and VGCCs are known to play a
significant role in controlling the release of transmitter from
presynaptic nerve terminals in the CNS. Because the gene mutation in
Cacnb4lh homozygotes results in loss of the beta 4 subunit's binding site
for ***alpha*** ***1*** subunits, we hypothesized that synaptic
transmission would be altered in the CNS of Cacnb4(lh) homozygotes. We
tested this hypothesis: by using whole cell recordings of single cells in
an in vitro slice preparation to investigate synaptic transmission in one
of the critical neuronal populations that generate seizure activity in
this strain, the somatosensory thalamus. The primary finding reported here
is the observation of a significant decrease in glutamatergic synaptic
transmission mediated by both N-methyl-D-aspartate (NMDA) and non-NMDA
receptors in somatosensory thalamic neurons of Cacnb4(lh) homozygotes
compared with matched, nonepileptic mice. In contrast, there was no
significant decrease in GABAergic transmission in Cacnb4lh homozygotes nor
was there any difference in effects mediated by presynaptic GABA,
receptors. We found a similar decrease in glutamatergic but not GABAergic
responses in Cacnb4(lh) homozygotes, suggesting that the independent
mutations in the two strains each affected P/Q channel function by causing
defective neurotransmitter release specific to glutamatergic synapses in
the somatosensory thalamus. This may bean important factor underlying the
generation of seizures in these models.

L6 ANSWER 33 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:175716 BIOSIS
DOCUMENT NUMBER: PREV199900175716
TITLE: Cloning and expression of a novel member of the low
voltage-activated ***T*** - ***type***
calcium ***channel*** family.
AUTHOR(S): Lee, Jung-Ha; Daud, Asif N.; Cribbs, Leanne L.; Lacerda,
Antonio E.; Pereverzev, Alexei; Klockner, Udo; Schneider,
Toni; Perez-Reyes, Edward (1)
CORPORATE SOURCE: (1) Deparment of Physiology, Loyola University Medical
Center, 2160 South First Avenue, Maywood, IL, 60153 USA
SOURCE: Journal of Neuroscience, (March 15, 1999) Vol. 19, No. 6,
pp. 1912-1921.
ISSN: 0270-6474.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Low voltage-activated Ca2+ channels play important roles in pacing
neuronal firing and producing network oscillations, such as those that
occur during sleep and epilepsy. Here we describe the cloning and
expression of the third member of the ***T*** - ***type*** family,
alpha1I or CavT.3, from rat brain. Northern analysis indicated that it is
predominantly expressed in brain. Expression of the cloned channel in
either Xenopus oocytes or stably transfected human embryonic kidney-293
cells revealed novel gating properties. We compared these
electrophysiological properties to those of the cloned ***T*** -
type channels alpha1G and alpha1H and to the high
voltage-activated channels formed by alpha1Ebeta3. The alpha1I channels
opened after small depolarizations of the membrane similar to alpha1G and
alpha1H but at more depolarized potentials. The kinetics of activation and
inactivation were dramatically slower, which allows the channel to act as
a Ca2+ injector. In oocytes, the kinetics were even slower, suggesting
that components of the expression system modulate its gating properties.
Steady-state inactivation occurred at higher potentials than any of the
other T channels, endowing the channel with a substantial window current. '
The alpha1I channel could still be classified as ***T*** - ***type***
by virtue of its criss-crossing kinetics, its slow deactivation (tail
current), and its small (11 pS) conductance in 110 mM Ba2+ solutions.
Based on its brain distribution and novel gating properties, we suggest
that alpha1I plays important roles in determining the electroresponsiveness of neurons, and hence, may be a novel drug target.

L6 ANSWER 34 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:180877 BIOSIS
DOCUMENT NUMBER: PREV199900180877
TITLE: Differential distribution of three members of a gene family
encoding low voltage-activated (***T*** - ***type***)
calcium ***channels*** .
AUTHOR(S): Talley, Edmund M. (1); Cribbs, Leanne L.; Lee, Jung-Ha;
Daud, Asif; Perez-Reyes, Edward; Bayliss, Douglas A.
CORPORATE SOURCE: (1) Department of Pharmacology, Health Sciences Center,
University of Virginia, Charlottesville, VA, 22908 USA
SOURCE: Journal of Neuroscience, (March 15, 1999) Vol. 19, No. 6,
pp. 1895-1911.
ISSN: 0270-6474.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Low voltage-activated (***T*** - ***type***) calcium currents are
observed in many central and peripheral neurons and display distinct
physiological and functional properties. Using in situ hybridization, we
have localized central and peripheral nervous system expression of three
transcripts (alpha1G, alpha1H, and alpha1I) of the ***T*** -
type ***calcium*** ***channel*** family (CavT). Each mRNA
demonstrated a unique distribution, and expression of the three genes was
largely complementary. We found high levels of expression of these
transcripts in regions associated with prominent ***T*** - ***type***
currents, including inferior olivary and thalamic relay neurons (which
expressed alpha1G), sensory ganglia, pituitary, and dentate gyrus granule
neurons (alpha1H), and thalamic reticular neurons (alpha1I and alpha1H).
Other regions of high expression included the Purkinje cell layer of the
cerebellum, the bed nucleus of the stria terminalis, the claustrum
(alpha1G), the olfactory tubercles (alpha1H and alpha1I), and the
subthalamic nucleus (alpha1I and alpha1G). Some neurons expressed high
levels of all three genes, including hippocampal pyramidal neurons and
olfactory granule cells. Many brain regions showed a predominance of
labeling for alpha1G, including the amygdala, cerebral cortex, rostral
hypothalamus, brainstem, and spinal cord. Exceptions included the basal
ganglia, which showed more prominent labeling for alpha1H and alpha1I, and
the olfactory bulb, the hippocampus, and the caudal hypothalamus, which
showed more even levels of all three transcripts. Our results are
consistent with the hypothesis that differential gene expression underlies
pharmacological and physiological heterogeneity observed in neuronal
T - ***type*** calcium currents, and they provide a molecular
basis for the study of ***T*** - ***type*** channels in particular
neurons.

L6 ANSWER 35 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:523019 SCISEARCH
THE GENUINE ARTICLE: 211VJ
TITLE: Low-voltage activated ***calcium*** ***channels***
: Achievements and problems
AUTHOR: Kostyuk P G (Reprint)
CORPORATE SOURCE: NATL ACAD SCI UKRAINE, AA BOGOMOLETS PHYSIOL INST,
UA-252601 KIEV, UKRAINE (Reprint)
COUNTRY OF AUTHOR: UKRAINE
SOURCE: NEUROSCIENCE, (JUL-AUG 1999) Vol. 92, No. 4, pp. 1157-1163
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,
LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0306-4522.
DOCUMENT TYPE: Editorial; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 84
*ABSTRACT IS AVAILABLE IN THE

ALL AND IALL FORMATS*
AB Low-voltage activated Ca2+ channels, which posses unique properties
quite different from those of common (high-voltage activated) channels,
were discovered lj years ago but the first ***alpha*** (***1***)
subunit has only recently been identified which might provide their
structural basis. However, simultaneously, extensive data are being
accumulated on the functional diversity of low-voltage activated Ca2+
currents with regard to their pharmacological sensitivity, ionic
selectivity, activation and inactivation kinetics. Such diversity
corresponds to equally prominent heterogeneity in the location and
function of the channels.
This commentary summarizes the data available in an attempt to predict
a possibly wider structural subdivision of low-voltage activated Ca2+
channels into subtypes. (C) 1999 IBRO. Published by Elsevier Science Ltd.

L6 ANSWER 36 OF 104 SCISEARCH
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ACCESSION NUMBER: 1999:627736 SCISEARCH
THE GENUINE ARTICLE: 224WJ
TITLE: Immunohistochemical detection of alpha 1E voltage-gated
Ca2+ channel isoforms in cerebellum, INS-1 cells, and
neuroendocrine cells of the digestive system
AUTHOR: Grabsch H; Pereverzev A; Weiergraber M; Schramm M; Henry
M; Vajna R; Beattie R E; Volsen S G; Klockner U; Hescheler
J; Schneider T (Reprint)
CORPORATE SOURCE: UNIV COLOGNE, INST NEUROPHYSIOL, ROBERT KOCH STR 39,
D-50931 COLOGNE, GERMANY (Reprint); UNIV COLOGNE, INST
NEUROPHYSIOL, D-50931 COLOGNE, GERMANY; UNIV COLOGNE, INST
VEGETAT PHYSIOL, D-50931 COLOGNE, GERMANY; KLININKUM
LEVERKUSEN, INST PATHOL, LEVERKUSEN, GERMANY; ELY LILLY &
CO, LILLY RES CTR, CNS RES, REB, SGV, WINDLESHAM, SURREY,
ENGLAND
COUNTRY OF AUTHOR: GERMANY; ENGLAND
SOURCE: JOURNAL OF HISTOCHEMISTRY & CYTOCHEMISTRY, (AUG 1999) Vol.
47, No. 8, pp. 981-993.
Publisher: HISTOCHEMICAL SOC INC, UNIV WASHINGTON, DEPT
BIOSTRUCTURE, BOX 357420, SEATTLE, WA 98195.
ISSN: 0022-1554.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 74
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Polyclonal antibodies were raised against a common and a specific
epitope present only in longer alpha 1E isoforms of voltage-gated Ca2+
channels, yielding an "anti-E-com" and an "anti-E-spec" serum,
respectively. The specificity of both sera was established by
immunocytochemistry and immunoblotting using stably transfected HEK-293
cells or membrane proteins derived from them. Cells from the insulinoma
cell line INS-1, tissue sections from cerebellum, and representative
regions of gastrointestinal tract were stained immunocytochemically. INS-1
cells expressed an alpha 1E splice variant with a longer carboxy terminus,
the so-called alpha 1Ee isoform. Similarily, in rat cerebellum, which was
used as a reference system, the anti-E-spec serum stained somata and
dendrites of Purkinje cells. Only faint staining was seen throughout the
cerebellar granule cell layer. After prolonged incubation times, neurons
of the molecular layer were stained by anti-E-com, suggesting that a
shorter alpha 1E isoform is expressed at a lower protein density. In human
gastrointestinal tract, endocrine cells of the antral mucosa (stomach),
small and large intestine, and islets of Langerhans were stained by the
anti-E-spec serum. In addition, staining by the anti-E-spec serum was
observed in Paneth cells and in the smooth muscle cell layer of the lamina
muscularis mucosae. We conclude that the longer alpha 1Ee isoform is
expressed in neuroendocrine cells of the digestive system and that, in
pancreas, alpha 1Ee expression is restricted to the neuroendocrine part,
the islets of Langerhans. alpha 1E therefore appears to be a common
voltage-gated Ca2+ channel linked to neuroendocrine and related systems of
the body.

L6 ANSWER 37 OF 104 MEDLINE
DUPLICATE 9
ACCESSION NUMBER: 2000044191 MEDLINE
DOCUMENT NUMBER: 20044191
TITLE: High-voltage-activated ***calcium*** ***channel***
messenger RNA expression in the 140-3 neuroblastoma-glioma
cell line.
AUTHOR: Gottschalk W; Kim D S; Chin H; Stanley E F
CORPORATE SOURCE: Synaptic Mechanisms Section, National Institutes of
Neurological Disorders and Stroke, National Institutes of
Health, Bethesda, MD 20892, USA.
SOURCE: NEUROSCIENCE, (1999) 94 (3) 975-83.
Journal code: NZR. ISSN: 0306-4522.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB Expression of ***calcium*** ***channel*** ***alpha1***
subunits in oocytes or cell lines has proven to be a powerful method in
the analysis of structure-function relations, but these experimental
systems are of limited value in the examination of neuron-specific
functions such as transmitter release. Cell lines derived from neurons are
often capable of these functions, but their intrinsic ***calcium***
channel ***alpha1*** subunits are complicating factors in
experimental design. We have examined the biophysical and molecular
properties of ***calcium*** ***channels*** in a little studied
neuroblastoma-glioma hybrid cell line, 140-3, a close relative of the
NG108-15 cell line, to test whether this cell line might serve a role as
an expression system for neural mechanisms. This cell was selected as it
contains an intact transmitter release mechanism yet secretes little in
response to depolarization. Patch-clamp recording revealed only a
prominent low-threshold, rapidly inactivating calcium current with a
single-channel conductance of approximately 7 pS that was identified as
T ***type*** . A search for ***calcium*** ***channel***
alpha1 subunit messenger RNA in the 140-3 cells with three
different tests only revealed alpha1C, whereas alpha1A-alpha1C were
present in the parent NG108-15 line. We made a particular effort to search
for alpha1E, since this subunit has been associated with a
low-voltage-activated current. Our findings suggest that, since the
principal nerve terminal-associated ***calcium*** ***channels***
(alpha1A, alpha1B, alpha1E) are absent in the 140-3 cell, this cell line
may prove a particularly useful model for the analysis of the role of
high-voltage-activated ***calcium*** ***channels*** in complex
functions of neuronal cells.

L6 ANSWER 38 OF 104 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999133651 EMBASE
TITLE: Voltage-operated Ca2+ channels and the acrosome reaction:
Which channels are present and what do they do?.
AUTHOR: Publicover S.J.; Barratt C.L.R.
CORPORATE SOURCE: S.J. Publicover, School of Biological Science, University
of Birmingham, Birmingham B15 2TT, United Kingdom
SOURCE: Human Reproduction, (1999) 14/4 (873-879).
Refs: 74
ISSN: 0268-1161 CODEN: HUREEE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 002 Physiology
028 Urology and Nephrology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Evidence from pharmacological studies suggests that induction of the
acrosome reaction of mammalian spermatozoa by solubilized zona pellucida,
and possibly by progesterone, is dependent upon Ca2+ influx through
voltage-operated Ca2+ channels. Studies on Ca2+ accumulation and membrane
potential in ligand-stimulated or artificially depolarized spermatozoa
support such a conclusion. Electrophysiological studies on rodent
spermatogenic cells have revealed the presence of a ' ***T*** '
type voltage-operated Ca2+ current. This current has
pharmacological attributes consistent with those of the putative channel
responsible for Ca2+ influx mediating the acrosome reaction. However, use
of molecular techniques to study human and rodent testis and spermatogenic
cells has detected the presence of three different voltage-operated Ca2+
channel subunits. One of these (. ***alpha*** . ***1*** (E)) may
generate T-currents, though this is currently disputed. Voltage-operated
Ca2+ channel structure and the relationship between channel subunit
expression and the characteristics of consequent Ca2+ currents is briefly
reviewed. The nature and function of T-channel-mediated Ca2+ influx is
examined in the contest of the time-course of ligand- and
depolarization-induced elevation of [Ca2+](i) in mammalian spermatozoa. It
is likely that a secondary Ca2+ response (mobilization of stored Ca2+ or
activation of a second Ca2+-influx pathway) is required for the acrosome
reaction. Evidence for the existence and participation

of various
candidates is discussed (including voltage-operated Ca2+ channels, which
may be functionally expressed only in mature spermatozoa), the available
evidence favouring a secondary Ca2+-influx pathway. Immediate priorities
for future research in this area are proposed.

L6 ANSWER 39 OF 104 MEDLINE
DUPLICATE 10
ACCESSION NUMBER: 1999127945 MEDLINE
DOCUMENT NUMBER: 99127945
TITLE: Structure and functional characterization of a novel human
low-voltage activated ***calcium*** ***channel*** .
AUTHOR: Williams M E; Washburn M S; Hans M; Urrutia A; Brust P F;
Prodanovich P; Harpold M M; Stauderman K A
CORPORATE SOURCE: SIBIA Neurosciences Inc., La Jolla, California 92037, USA.
SOURCE: JOURNAL OF NEUROCHEMISTRY, (1999 Feb) 72 (2) 791-9.
Journal code: JAV. ISSN: 0022-3042.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF073931
ENTRY MONTH: 199904
AB We have isolated and characterized overlapping cDNAs encoding a novel,
voltage-gated Ca2+ channel ***alpha1*** subunit, alpha1H, from a human
medullary thyroid carcinoma cell line. The alpha1H subunit is structurally
similar to previously described ***alpha1*** subunits. Northern blot
analysis indicates that alpha1H mRNA is expressed throughout the brain,
primarily in the amygdala, caudate nucleus, and putamen, as well as in
several nonneuronal tissues, with relatively high levels in the liver,
kidney, and heart. Ba2+ currents recorded from human embryonic kidney 293
cells transiently expressing alpha1H activated at relatively
hyperpolarized potentials (-50 mV), rapidly inactivated (tau = 17 ms), and
slowly deactivated. Similar results were observed in Xenopus oocytes
expressing alpha1H. Single-channel measurements in human embryonic kidney
293 cells revealed a single-channel conductance of approximately 9 pS.
These channels are blocked by Ni2+ (IC50 = 6.6 microM) and the ***T***
- ***type*** channel antagonists mibefradil (approximately 50% block at
1 microM) and amiloride (IC50 = 167 microM). Thus, alpha1H-containing
channels exhibit biophysical and pharmacological properties characteristic
of low voltage-activated, or ***T*** - ***type*** , Ca2+ channels.

L6 ANSWER 40 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:278507 SCISEARCH
THE GENUINE ARTICLE: 183CV
TITLE: A ***T*** - ***type*** ***calcium***
channel from mouse brain
AUTHOR: Klugbauer N (Reprint); Marais E; Lacinova L; Hofmann F
CORPORATE SOURCE: TECH UNIV MUNICH, INST PHARMAKOL & TOXIKOL, BIEDERSTEINER
STR 29, D-80802 MUNICH, GERMANY (Reprint); SLOVAK ACAD
SCI, INST MOL PHYSIOL & GENET, BRATISLAVA 83304, SLOVAKIA
COUNTRY OF AUTHOR: GERMANY; SLOVAKIA
SOURCE: PFLUGERS ARCHIV-EUROPEAN JOURNAL OF PHYSIOLOGY, (APR 1999)
Vol. 437, No. 5, pp. 710-715.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY
10010.
ISSN: 0031-6768.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB A member of the low-voltage-activated ***calcium*** ***channel***
family was identified in mouse brain by taking advantage of amino acid
sequences that have been evolutionary conserved. The identified sequence
is similar to that of the recently cloned rat alpha(1G) ***T*** -
type ***calcium*** ***channel*** , but there are
differences in two insertions in the intracellular connecting loops.
Northern blot analysis indicates that its expression is strong in the
brain. In situ hybridization revealed that, in mouse brain, the alpha(1G)
mRNA is found in the cerebellum, hippocampus, thalamus and olfactory bulb.
In contrast to L-type ***calcium*** ***channel*** currents, I-Ba
and I-Ca through the alpha(1G) channel expressed in HEK293 cells did not
differ in terms of current density, voltage dependence of current
activation, inactivation and deactivation, and speed of recovery from
voltage-dependent inactivation. The kinetics of I-Ca inactivation were
significantly slower than those of I-Ba. The expressed alpha(1G) channel
has a relatively high sensitivity to mibefradil, but is only slightly
affected by Ni2+.

L6 ANSWER 41 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:247247 BIOSIS
DOCUMENT NUMBER: PREV199900247247
TITLE: Absence of modulation of the expressed ***calcium***
channel alpha1G subunit by alpha2delta subunits.
AUTHOR(S): Lacinova, L. (1); Klugbauer, N.; Hofmann, F.
CORPORATE SOURCE: (1) Institut fuer Pharmakologie und Toxikologie der
Technischen Universitaet Muenchen, Biedersteiner Strasse
29, 80802, Muenchen Germany
SOURCE: Journal of Physiology (Cambridge), (May 1, 1999) Vol. 516,
No. 3, pp. 639-645.
ISSN: 0022-3751.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB 1. The modulatory action of the alpha2delta subunit on various
high-voltage-activated ***calcium*** ***channels*** has been
demonstrated previously. However, very little is known about auxiliary
subunit modulation of low-voltage-activated (LVA) ***calcium***
channels . We have examined the modulation of the alpha1G subunit
corresponding to the neuronal ***T*** - ***type*** ***calcium***
channel by the ubiquitously expressed alpha2delta-1 and
brain-specific alpha2delta-3 subunits. 2. The alpha1G subunit was
expressed alone or in combination with either the alpha2delta-1 or
alpha2delta-3 subunit in human embryonic kidney (HEK 293) cells and
whole-cell barium currents were measured. The current density-voltage
relationships for peak and sustained current, kinetics of current
activation and inactivation, voltage dependence of current inactivation
and time course of the recovery from inactivation were analysed for each
type of expressed channel. No significant difference was found for any of
the examined parameters. 3. These results suggest that the LVA alpha1G
channel is not regulated by known auxiliary alpha2delta subunits.

L6 ANSWER 42 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:467531 SCISEARCH
THE GENUINE ARTICLE: 205MM
TITLE: Isoforms of alpha 1E voltage-gated ***calcium***
channels in rat cerebellar granule cells -
Detection of major ***calcium*** ***channel***
alpha ***1*** -transcripts by reverse
transcription-polymerase chain reaction
AUTHOR: Schramm M; Vajna R; Pereverzev A; Tottene A; Klockner U;
Pietrobon D; Hescheler J; Schneider T (Reprint)
CORPORATE SOURCE: UNIV COLOGNE, INST NEUROPHYSIOL, ROBERT KOCH STR 39,
D-50931 COLOGNE, GERMANY (Reprint); UNIV COLOGNE, INST
NEUROPHYSIOL, D-50931 COLOGNE, GERMANY; UNIV COLOGNE, INST
VEGETAT PHYSIOL, D-50931 COLOGNE, GERMANY; UNIV PADUA,
DEPT BIOMED SCI, I-35121 PADUA, ITALY
COUNTRY OF AUTHOR: GERMANY; ITALY
SOURCE: NEUROSCIENCE, (JUN 1999) Vol. 92, No. 2, pp. 565-575.
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD,
LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
ISSN: 0306-4522.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 35
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB In primary cultures of rat cerebellar granule cells, transcripts of
voltage-gated Ca2+ channels have been amplified by reverse
transcription-polymerase chain reaction and identified by sequencing of
subcloned polymerase chain reaction products. In these neurons cultured
for six to eight days in vitro, fragments of the three major transcripts
alpha 1C, alpha 1A, and alpha 1E are detected using degenerated
oligonucleotide primer pairs under highly stringent conditions. Whole-cell
Ca2+ current recordings from six to eight days in vitro granule cells show
that most of the current is due to L-type (25%), P-type (33%) and R-type
(30%) Ca2+; channels. These data support the correlation between alpha 1A
and P-type Ca2+ channels (G1) and between alpha 1E and R-type channels (G2
and G3). By including specific primer pairs for alpha 1E the complimentary
DNA fragments of indicative regions of alpha 1E isoforms are amplified
corresponding to the three most variable regions of alpha 1E, the 5'-end,
the II/III-loop, and the central part of the 3'-end. Although the
complementary DNA fragments of the 5'-end of rat alpha 1E yield a uniform

reverse transcription-polymerase chain reaction product, its structure is unusual in the sense that it is longer than in the cloned rat alpha 1E complementary DNA. It corresponds to the alpha 1E isoform reported for mouse and human brain and is also expressed in cerebellum and cerebrum of rat brain as the major or maybe even the only variant of alpha 1E. While fragments of a new rat alpha 1E isoform are amplified from the 5'-end, three known fragments of the II/III-loop and two known isoforms homologue to the 3'-coding region are detected, which in the last case are discriminated by a 129 base pair insertion. The shift of the alpha 1E expression from a pattern seen in cerebellum (alpha 1Ee) to a pattern identified in other regions of the brain (alpha 1E-3) is discussed. These data show that: (i) alpha 1E is expressed in rat brain as a structural homologue to the mouse and human alpha 1E; and (ii) rat cerebellar granule cells in primary culture express a set of alpha 1E isoforms, containing two different sized carboxy termini. Since no new transcripts of high-voltage-activated Ca2+ channels genes are identified using degenerate oligonucleotide primer pairs, the two isoforms differentiated by the 129 base pair insertion might correspond to the two R-type channels, G2 and G3, characterized in these neurons. Functional studies including recombinant cells with the different proposed isoforms should provide more evidence for this conclusion. (C) 1999 IBRO. Published by Elsevier Science Ltd.

L6 ANSWER 43 OF 104 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1999448596 MEDLINE
DOCUMENT NUMBER: 99448596
TITLE: Osteoblasts derived from load-bearing bones of the rat express both L- and T-like voltage-operated ***calcium*** ***channels*** and mRNA for alpha 1C, alpha 1D and alpha 1G subunits.
AUTHOR: Gu Y; Preston M R; el Haj A J; Hamid J; Zamponi G W; Howl J; Publicover S J
CORPORATE SOURCE: School of Biological Sciences, University of Birmingham, UK.
SOURCE: PFLUGERS ARCHIV. EUROPEAN JOURNAL OF PHYSIOLOGY, (1999 Sep) 438 (4) 553-60.
Journal code: OZX. ISSN: 0031-6768.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY WEEK: 20000104
AB Voltage operated ***calcium*** ***channels*** (VOCCs) are implicated in osteoblastic mechano- and hormonal transduction. Very little, however, is known about the expression of VOCCs in osteoblasts of load-bearing bones. Here we describe two types of whole-cell calcium current in rat femoral explant-derived osteoblasts. The first is high-voltage activated and sensitive to nifedipine, Bay K8644 and FPL 64176. The second is low-voltage activated and is sensitive to micromolar concentrations of Ni2+. The properties of these two currents are consistent with those of L-type and ***T*** - ***type*** calcium currents respectively. ***T*** - ***type*** currents were detected in most cells on the day of passage, the level of expression being significantly lower on subsequent days. L-type currents were also most common on the day of passage but were detected consistently throughout the 4-day period of study. The reverse transcription polymerase chain reaction with non-specific primers directed against all L-type VOCC ***alpha*** ***1*** subunits and then with specific primers directed against sequences from rat brain alpha 1C (L-type), alpha 1D (L-type) and alpha 1G (***T*** - ***type***) VOCC subunits detected transcripts of appropriate size in all four cases. Products from the three sets of specific primer pairs (alpha 1C, alpha 1D, alpha 1G) were sequenced and were identical to their respective rat brain templates.

L6 ANSWER 44 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:338939 CAPLUS
DOCUMENT NUMBER: 131:156147
TITLE: Molecular diversity of voltage-sensitive ***calcium*** ***channels*** in smooth muscle cells
AUTHOR(S): Bielefeldt, Klaus
CORPORATE SOURCE: Department of Internal Medicine, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: J. Lab. Clin. Med. (1999), 133(5), 469-477
CODEN: JLCMAK; ISSN: 0022-2143
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Voltage-sensitive ***calcium*** ***channels*** play an important role in the excitation-contraction coupling of smooth muscle. Several subunits form the oligomeric channel complex and det. its functional properties. Therefore a differential distribution of the various channel subunits and their splice forms could contribute to the functional specialization of smooth muscle cells. To test this hypothesis, specific primers were designed to amplify mRNA from vascular and gastrointestinal smooth muscle of the rabbit by reverse transcription and polymerase chain reaction (RT-PCR). The presence of high- and low-threshold voltage-dependent ***calcium*** ***channels*** was also examd. in a smooth muscle-derived cell line (A7R5). Consistent with the physiol. data, smooth muscle contains mRNA for the pore-forming subunits of high- and low-threshold voltage-dependent ***calcium*** ***channels*** , .alpha.-1C and .alpha.-1G. Three splice variants of the .alpha.-1C-subunit were identified in smooth muscle. These may affect dihydropyridine binding and the interaction between the .alpha.-1C and the .beta.-subunit. In addn., three of the four cloned .beta.-subunits (.beta.-1b, .beta.-2, and .beta.-3) could be found in all smooth muscle tissues examd. These data demonstrate that various splice forms of the L-type ***calcium*** ***channel*** exist in smooth muscle tissue. Moreover, these expts. also show for the first time that smooth muscle cells contain mRNA for low-threshold voltage-sensitive ***calcium*** ***channels*** . Combinations of the pore-forming subunits with one of the three .beta.-subunits could account for functional differences between smooth muscle cells from distinct regions. A better understanding of the structure and function of these channels may help in our understanding of diseases affecting smooth muscle and help in the development of novel drugs targeting these mols.
REFERENCE COUNT: 27
REFERENCE(S): (1) Ackerman, M; N Engl J Med 1997, V336, P1575 CAPLUS
(2) Biel, M; Eur J Biochem 1991, V200, P81 CAPLUS
(4) Chomczynski, P; Anal Biochem 1987, V162, P156 CAPLUS
(5) de Waard, M; Ion channels 1996, V4, P41 CAPLUS
(6) Feron, O; Eur J Biochem 1994, V222, P195 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 45 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:522816 SCISEARCH
THE GENUINE ARTICLE: 211TD
TITLE: Discrete regional distributions suggest diverse functional roles of ***calcium*** ***channel*** a, subunits in sperm
AUTHOR: Westenbroek R E; Babcock D F (Reprint)
CORPORATE SOURCE: UNIV WASHINGTON, DEPT PHYSIOL & BIOPHYS 357290, SEATTLE, WA 98195 (Reprint); UNIV WASHINGTON, DEPT PHYSIOL & BIOPHYS 357290, SEATTLE, WA 98195; UNIV WASHINGTON, DEPT PHARMACOL, SEATTLE, WA 98195
COUNTRY OF AUTHOR: USA
SOURCE: DEVELOPMENTAL BIOLOGY, (15 MAR 1999) Vol. 207, No. 2, pp. 457-469.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 0012-1606.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 67
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The Ca channels of male germ-line cells are partially characterized, but the molecular properties and subcellular localization of the Ca channels of mature sperm are unknown. Here, we probe rodent sperm with anti-peptide antibodies directed to cytosolic domains of cloned rat brain alpha(1A), alpha(1C), and alpha(1E) Ca channel subunits. Each recognizes a 200- to 245-kDa band on immunoblots of whole rat sperm extracts. A smaller (similar to 110-kDa) alpha(1C) band also is detected. Confocal fluorescence images of mouse sperm show characteristic patterns of punctate alpha(1A)-, alpha(1C)-, and alpha(1E)-immunoreactivity. For alpha(1A) the puncta are larger, less numerous, and more variable in distribution than for alpha(1C) and alpha(1E). They are absent from the acrosomal crescent, but are present elsewhere over the sperm head, often at the apical tip and equatorial segment. They also are found at irregular intervals along both the midpiece and the principal piece of the flagellum. For alpha(1C) and alpha(1E), puncta are dense along dorsal and

ventral aspects of the acrosomal cap. For alpha(1E) but not alpha(1C), the
remainder of the acrosomal region also is labeled. Neither is found in the
postacrosomal region or on the midpiece. Puncta of alpha(1C) and alpha(1E)
occur at regular intervals each in two parallel rows, at the dorsal and
ventral aspects of the proximal segment of the flagellar principal piece.
The puncta in these arrays become less abundant and intense in the distal
flagellum. These results demonstrate that multiple Ca channel proteins are
present in mature sperm and are regionally localized in ways that may give
them different regulatory roles. (C) 1999 Academic Press.

L6 ANSWER 46 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12
ACCESSION NUMBER: 1999:186400 BIOSIS
DOCUMENT NUMBER: PREV199900186400
TITLE: Cloning of the rat beta-cell ***T*** - ***type***
calcium ***channel*** ***alpha1*** subunit
and its regulation by glucose.
AUTHOR(S): Zhuang, H. (1); Hu, F.; Bhattacharjee, A.; Zhang, M.; Wu,
S.; Berggren, P.-O.; Li, M.
CORPORATE SOURCE: (1) Dept of Pharmacology, University of South Alabama
College of Medicine, Mobile, AL USA
SOURCE: Biophysical Journal, (Jan., 1999) Vol. 76, No. 1 PART 2,
pp. A409.
Meeting Info.: Forty-third Annual Meeting of the
Biophysical Society Baltimore, Maryland, USA February
13-17, 1999
ISSN: 0006-3495.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 47 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:193964 BIOSIS
DOCUMENT NUMBER: PREV199900193964
TITLE: Arachidonic acid modulation of alpha1H, a cloned human
T - ***type*** ***calcium*** ***channel***
AUTHOR(S): Zhang, Yi (1); Cribbs, Leanne L.; Perez-Reyes, Edward;
Satin, Jonathan
CORPORATE SOURCE: (1) Dept of Physiology, Univ. of Kentucky Col of Med,
Lexington, KY, 40536-0298 USA
SOURCE: Biophysical Journal, (Jan., 1999) Vol. 76, No. 1 PART 2,
pp. A408.
Meeting Info.: Forty-third Annual Meeting of the
Biophysical Society Baltimore, Maryland, USA February
13-17, 1999
ISSN: 0006-3495.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 48 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)DUPLICATE 13
ACCESSION NUMBER: 1999:278944 SCISEARCH
THE GENUINE ARTICLE: 183DU
TITLE: Identification of structural elements of the
testis-specific voltage dependent ***calcium***
channel that potentially regulate its biophysical
properties
AUTHOR: Goodwin L O (Reprint); Leeds N B; Guzowski D; Hurley I R;
Pergolizzi R G; Benoff S
CORPORATE SOURCE: NYU, N SHORE UNIV HOSP, SCH MED, DEPT RES, MANHASSET, NY 11030 (Reprint); NYU, N SHORE UNIV HOSP, SCH MED, DEPT OBSTET & GYNECOL, MANHASSET, NY 11030; NYU, SCH MED, DEPT CELL BIOL, MANHASSET, NY
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR HUMAN REPRODUCTION, (APR 1999) Vol. 5, No. 4, pp. 311-322.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 1360-9947.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 98
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Calcium influx through voltage-dependent ***calcium***
channels regulates the physiological acrosome reaction of
mammalian spermatozoa. Expression of the mRNA for these voltage-dependent
calcium ***channels*** and its co-ordinated translation is
initiated early in rat mate germ line development and continues throughout
spermatogenesis. Herein, we report the complete mRNA and deduced amino
acid sequence of the ***alpha*** ***1*** (C) pore-forming subunit
of the rat testis-specific L-type ***calcium*** ***channel*** .
This subunit is transcribed from the ***alpha*** ***1*** (C) gene,
which is also expressed in brain and cardiac muscle. The cardiac- and
testis-specific isoforms of the ale subunit are produced by alternate
splicing of the same primary transcript. The testis-specific isoform
differs from that of cardiac tissue at its amino terminus and in
transmembrane segments IS6, IIIS2 and IVS3, which are also dihydropyridine
binding sites. In somatic tissues, segments S2 and S3 regulate channel
activation while the amino terminus and segment IS6 contribute to channel
inactivation kinetics. The amino terminus and IS6 segment of the
testis-specific ***alpha*** ***1*** (C) subunit are also expressed
respectively, in the brain and in smooth muscle from lung where they alter
the electrophysiological characteristics of the subunit to produce
relatively slow inactivation kinetics. These findings provide a molecular
explanation for the detection by others, by patch clamp analysis, of
T - ***type*** calcium currents in immature spermatogenic cells
and of atypical L-type calcium currents in mature spermatozoa.

L6 ANSWER 49 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:424815 SCISEARCH
THE GENUINE ARTICLE: 201BN
TITLE: beta subunit reshuffling modifies N- and P/Q-type Ca2+
channel subunit compositions in lethargic mouse brain
AUTHOR: Burgess D L; Biddlecome G H; McDonough S I; Diaz M E;
Zilinski C A; Bean B P; Campbell K P; Noebels J L
(Reprint)
CORPORATE SOURCE: BAYLOR COLL MED, DEPT NEUROL, HOUSTON, TX 77030 (Reprint); BAYLOR COLL MED, DEPT NEUROL, HOUSTON, TX 77030; BAYLOR COLL MED, DEPT MOL & HUMAN GENET, HOUSTON, TX 77030; UNIV IOWA, COLL MED, HOWARD HUGHES MED INST, DEPT PHYSIOL & BIOPHYS, DEPT NEUROL, IOWA CITY, IA 52242; HARVARD UNIV, SCH MED, DEPT NEUROBIOL, BOSTON, MA 02115
COUNTRY OF AUTHOR: USA
SOURCE: MOLECULAR AND CELLULAR NEUROSCIENCE, (APR 1999) Vol. 13, No. 4, pp. 293-311.
Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
ISSN: 1044-7431.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 68
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Neuronal voltage-dependent Ca2+ channels are heteromultimers of
alpha (***1***), beta, and alpha(2)delta subunits, and any one
of five ***alpha*** (***1***) subunits (alpha(1A-E)) may associate
with one of four beta subunits (beta(1-4)) The specific ***alpha*** (
1)-beta combination assembled determines single-channel
properties, while variation in the proportion of each combination
contributes to the functional diversity of neurons. The mouse mutant
lethargic (lh) exhibits severe neurological defects due to a mutation that
deletes the ***alpha*** (***1***) subunit interaction domain of the
beta(4) subunit. Since beta subunits regulate critical ***alpha*** (
1) subunit properties in heterologous expression systems, loss of
beta(4) in lethargic could dramatically alter channel localization and
behavior unless beta(1-3), subunits can be used as substitutes in vivo.
Here we demonstrate increased steady-state associations of alpha(1A) and
alpha(1B) with the remaining beta(1-3), subunits, without significant
changes in beta(1-3), mRNA abundance. The immunolocalization of alpha(1A)
and alpha(1B) protein in lethargic brain is indistinguishable from
wild-type by light microscopy. Furthermore, the measurement of
large-amplitude beta-type currents in dissociated lethargic Purkinje
neurons indicates that these alpha(1A)-containing channels retain
regulation by beta subunits. We conclude that several properties of
alpha(1A) and alpha(1B) proteins are not uniquely regulated by beta(4) in
vivo and may be rescued by beta(1-3) subunit reshuffling. The complex
neurological manifestation of the lethargic mutation therefore emerges
from loss of beta(4) coupled with the widespread pairing of surrogate beta
subunits with multiple Ca2+ channel subtypes. The existence of beta
subunit reshuffling demonstrates that molecular plasticity of Ca2+ channel
assembly, a normal feature of early brain development, is retained in the
mature brain.

L6 ANSWER 50 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 2000:66974 BIOSIS
DOCUMENT NUMBER: PREV200000066974
TITLE: Identification of human alpha1G
T - ***type***
calcium ***channel*** splice variants.
AUTHOR(S): Monteil, A. (1); Chemin, J. (1); Spiesser, S. (1);
Bourinet, E. (1); Lory, P. (1); Nargeot, J.

(1)
CORPORATE SOURCE: (1) Institut de Genetique Humaine, CNRS UPR1142, 141 Rue de
la Cardonille, 34396, Montpellier France
SOURCE: Society for Neuroscience Abstracts, (1999) Vol. 25, No.
1-2, pp. 197.
Meeting Info.: 29th Annual Meeting of the Society for
Neuroscience, Part 1 Miami Beach, Florida, USA October
23-28, 1999 The Society for Neuroscience . ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 51 OF 104 MEDLINE DUPLICATE 14
ACCESSION NUMBER: 2000014446 MEDLINE
DOCUMENT NUMBER: 20014446
TITLE: Structure and alternative splicing of the gene encoding
alpha1G, a human brain T ***calcium*** ***channel***
alpha1 subunit.
AUTHOR: Mittman S; Guo J; Agnew W S
CORPORATE SOURCE: Department of Anesthesiology, The Johns Hopkins University
School of Medicine, Baltimore, MD 21287, USA..
smittman@jhmi.edu
CONTRACT NUMBER: K08NS01939 (NINDS)
P50HL52307 (NHLBI)
SOURCE: NEUROSCIENCE LETTERS, (1999 Oct 29) 274 (3) 143-6.
Journal code: N7N. ISSN: 0304-3940.
PUB. COUNTRY: Ireland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AC004590; GENBANK-AF027984; GENBANK-R43876;
GENBANK-R40146; GENBANK-R43935; GENBANK-R46109;
GENBANK-AF134985; GENBANK-AF134986
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB The structure of CACNA1G, the gene encoding alpha1G, a human brain T Ca2+
channel ***alpha1*** subunit, was determined by comparison of
polymerase chain reaction-amplified brain cDNA and genomic sequences. The
gene consists of at least 38 exons, two of them newly-identified, spanning
at least 66490 basepairs of chromosome 17q22. Alternative splicing of the
RNA occurs at six sites: cassette exons 14, 26, 34 and 35, an internal
donor in exon 25 and protein-coding intron 38B. Additionally, the RNA can
be polyadenylated at either of two sites. Alternative splicing of CACNA1G
RNA may lead to expression of as many as 24 distinct protein products,
ranging from 2171 to 2377 amino-acids residues.

L6 ANSWER 52 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)DUPLICATE 15
ACCESSION NUMBER: 1999:543509 SCISEARCH
THE GENUINE ARTICLE: 213WQ
TITLE: Structure and alternative splicing of the gene encoding
alpha(1I), a human brain T ***calcium***
channel ***alpha*** (***1***) subunit
AUTHOR: Mittman S (Reprint); Guo J; Emerick M C; Agnew W S
CORPORATE SOURCE: JOHNS HOPKINS UNIV, SCH MED, DEPT ANESTHESIOL, BALTIMORE,
MD 21287 (Reprint); JOHNS HOPKINS UNIV, SCH MED, DEPT
PHYSIOL, BALTIMORE, MD 21287; JOHNS HOPKINS UNIV, SCH MED,
DEPT NEUROSCI, BALTIMORE, MD 21287
COUNTRY OF AUTHOR: USA
SOURCE: NEUROSCIENCE LETTERS, (16 JUL 1999) Vol. 269, No. 3, pp.
121-124.
Publisher: ELSEVIER SCI IRELAND LTD, CUSTOMER RELATIONS
MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE,
IRELAND.
ISSN: 0304-3940.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 18
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The structure of CACNA1I, the gene encoding alpha(1I), a human brain T
Ca2+ channel ***alpha*** (***1***) subunit, was determined by
comparison of polymerase chain reaction-amplified brain cDNA and genomic
sequences. The gene consists of at least 36 exons spanning at least 115
168 basepairs of chromosome 22q12.3-13.2. The predicted protein has 2016
amino acids and 28 potential phosphorylation sites. Alternative splicing
of the gene occurs at two sites: cassette exon 9 and an alternative
acceptor in exon 33. Molecular diversity generated by alternative splicing
and post-translational modification of this and other members of the T
alpha (***1***) subunit gene family may account for the
observed heterogeneity of T currents in central neurons. (C) 1999 Elsevier
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L6 ANSWER 53 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:752638 SCISEARCH
THE GENUINE ARTICLE: 241BD
TITLE: Single gene defects in mice: the role of voltage-dependent
calcium ***channels*** in absence models
AUTHOR: Burgess D L (Reprint); Noebels J L
CORPORATE SOURCE: BAYLOR COLL MED, DEPT NEUROL, 1 BAYLOR PLAZA, HOUSTON, TX
77303 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: EPILEPSY RESEARCH, (SEP 1999) Vol. 36, No. 2-3, Sp. iss.
SI, pp. 111-122.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE
AMSTERDAM, NETHERLANDS.
ISSN: 0920-1211.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 102
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Nineteen genes encoding ***alpha*** (***1***), beta, gamma, or
alpha(2)delta voltage-dependent ***calcium*** ***channel***
subunits have been identified to date. Recent studies have found that
three of these genes are mutated in mice with generalised cortical
spike-wave discharges (models of human absence epilepsy), emphasising the
importance of ***calcium*** ***channels*** in regulating the
expression of this inherited seizure phenotype. The tottering (tg) locus
encodes the ***calcium*** ***channel*** ***alpha*** (***1***)
subunit gene Cacna1a, lethargic (lh) encodes the beta subunit gene
Cacnb4, and stargazer (stg) encodes the (gamma) over dot subunit gene
Cacng2. These ***calcium*** ***channel*** mutants should provide
important insights into the basic mechanisms of neuronal synchronisation,
and the genes may be considered candidates for involvement in similar
human disorders. The mutant models offer an important opportunity to
elucidate the molecular, developmental, and physiological mechanisms
underlying one subtype of absence epilepsy. Since ***calcium***
channels are involved in numerous cellular functions, including
proliferation and differentiation, membrane excitability, neurite
outgrowth and synaptogenesis, signal transduction, and gene expression,
their role in generating the absence epilepsy phenotype may be complex. A
comparative analysis of channel function and neural excitability patterns
in tottering, lethargic, and stargazer brain should be useful in
identifying the common elements of ***calcium*** ***channel***
involvement in these absence models. (C) 1999 Elsevier Science B.V. All
rights reserved.

L6 ANSWER 54 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:671156 SCISEARCH
THE GENUINE ARTICLE: 230GW
TITLE: Anion channel blockers differentially affect ***T*** -
type Ca2+ currents of mouse spermatogenic cells,
alpha 1E currents expressed in Xenopus oocytes and the
sperm acrosome reaction
AUTHOR: Espinosa F; LopezGonzalez I; Serrano C J; Gasque G;
delaVegaBeltran J; Trevino C L; Darszon A (Reprint)
CORPORATE SOURCE: UNIV NACL AUTONOMA MEXICO, INST BIOTECHNOL, DEPT GENET &
FIS MOL, APDO 510-3, CUERNAVACA 62271, MORELOS, MEXICO
(Reprint); UNIV NACL AUTONOMA MEXICO, INST BIOTECHNOL,
DEPT GENET & FIS MOL, CUERNAVACA 62271, MORELOS, MEXICO
COUNTRY OF AUTHOR: MEXICO
SOURCE: DEVELOPMENTAL GENETICS, (AUG 1999) Vol. 25, No. 2, pp.
103-114.
Publisher: WILEY-LISS, DIV JOHN WILEY & SONS INC, 605
THIRD AVE, NEW YORK, NY 10158-0012.
ISSN: 0192-253X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 62
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The direct electrophysiological characterization of sperm Ca2+ channels
has been precluded by their small size and flat shape. An alternative to
study these channels is to use spermatogenic cells, the progenitors of
sperm, which are larger and easier to patch-clamp. In mouse and rat, the
only voltage-dependent Ca2+ currents displayed by these cells are of the
T ***type*** . Because com pounds that block these currents
inhibit the zona pellucida-induced Ca2+ uptake and the sperm acrosome
reaction (AR) at similar concentrations, it is likely that they are
fundamental for this process. Recent single channel recordings in mouse
sperm demonstrated the presence of a Cl- channel. This channel and the

zona pellucida (ZP)-induced AR were inhibited by niflumic acid (NA), an
anion channel blocker [Espinosa et al. (1998): FEBS lett 426:47-51].
Because NA and other onion channel blockers modulate cationic channels as
well, it became important to determine whether they affect the ***T*** - ***type*** Ca2+ currents of spermatogenic cells. These currents were
blocked in a voltage-dependent manner by NA, 1,9-dideoxyforskolin (DDF),
and 5-nitro-2-(3-phenylpropylamine)benzoic acid (NPPB). The IC50 values at
-20 mV were 43 mu M For NA, 28 mu M for DDF, and 15 mu M for NPPB.
Moreover, DDF partially inhibited the ZP-induced AR (40% at 1 mu M) and
NPPB displayed on IC50 value of 6 mu M For this reaction. These results
suggest that NA and DDF do not inhibit the ZP-induced AR by blocking
T - ***type*** Ca2+ currents, while NPPB may do so.
Interestingly 200 mu M NA was basically unable to inhibit alpha 1E Ca2+
channels expressed in Xenopus oocytes, questioning that this alpha subunit
codes for the ***T*** - ***type*** Ca2+ channels present in
spermatogenic cells. Evidence for the presence of alpha 1C, alpha 1G, and
alpha 1H in mouse pachytene spematocytes and in round and condensing
spermatids is presented. Dev. Genet. 25:103-114, 1999. (C) 1999
Wiley-Liss, Inc.

L6 ANSWER 55 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:686486 SCISEARCH
THE GENUINE ARTICLE: 232KP
TITLE: The effect of alpha 2-delta and other accessory subunits
on expression and properties of the ***calcium*** ***channel*** alpha 1G
AUTHOR: Dolphin A C (Reprint); Wyatt C N; Richards J; Beattie R E;
Craig P; Lee J H; Cribbs L L; Volsen S G; PerezReyes E
CORPORATE SOURCE: UNIV LONDON UNIV COLL, DEPT PHARMACOL, GOWER ST, LONDON
WC1E 6BT, ENGLAND (Reprint); LILLY RES CTR LTD, WINDLESHAM
GU20 6PH, SURREY, ENGLAND; LOYOLA UNIV, MED CTR, DEPT
PHYSIOL, MAYWOOD, IL 60153
COUNTRY OF AUTHOR: ENGLAND; USA
SOURCE: JOURNAL OF PHYSIOLOGY-LONDON, (15 AUG 1999) Vol. 519, No.
1, pp. 35-45.
Publisher: CAMBRIDGE UNIV PRESS, 40 WEST 20TH STREET, NEW
YORK, NY 10011-4211.
ISSN: 0022-3751.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 42
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB 1. The effect has been examined of the accessory alpha 2-delta and beta
subunits on the properties of alpha 1G-currents expressed in monkey COS-7
cells and Xenopus oocytes.
2. In immunocytochemical experiments, the co-expression of alpha
2-delta increased plasma membrane localization of expressed alpha 1G and
conversely the heterologous expression of alpha 1G increased
immunostaining for endogenous alpha 2-delta, suggesting an interaction
between the two subunits.
3. Heterologous expression of alpha 2-delta together with alpha 1G in
COS-7 cells increased the amplitude of expressed alpha 1G currents by
about 2-fold. This finding was confirmed in the Xenopus oocyte expression
system. The truncated delta construct did not increase alpha 1G current
amplitude, or increase its plasma membrane expression. This indicates that
it is the exofacial alpha 2 domain that is involved in the enhancement by
alpha 2-delta.
4. beta 1b also produced an increase of functional expression of alpha
1G, either in the absence or the presence of heterologously expressed
alpha 2-delta, whereas the other beta subunits had much smaller effects.
5. None of the accessory subunits had any marked influence on the
voltage dependence or kinetics of the expressed alpha 1G currents. These
results therefore suggest that alpha 2-delta and beta 1b interact with
alpha 1G to increase trafficking of, or stabilize, functional alpha 1G
channels expressed at the plasma membrane.

L6 ANSWER 56 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
ACCESSION NUMBER: 2000:85729 BIOSIS
DOCUMENT NUMBER: PREV200000085729
TITLE: Determinants of voltage-dependent inactivation affect
Mibefradil block of ***calcium*** ***channels*** .
AUTHOR(S): Jimenez, Cristina; Bourinet, Emmanuel; Leuranguer, Valerie;
Richard, Sylvain; Snutch, Terry P.; Nargeot, Joel (1)
CORPORATE SOURCE: (1) Institut de Genetique Humaine, CNRS UPR1142, 141 Rue de
la Cardonille, 34396, Montpellier Cedex 5 France
SOURCE: Neuropharmacology, (Dec. 17, 1999) Vol. 39, No. 1, pp.
1-10.
ISSN: 0028-3908.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The voltage gated ***calcium*** ***channel*** family is a major
target for a range of therapeutic drugs. Mibefradil (Ro 40-5967) belongs
to a new chemical class of these molecules which differs from other Ca2+
antagonists by its ability to potently block ***T*** - ***type***
Ca2+ channels. However, this molecule has also been shown to inhibit other
Ca2+ channel subtypes. To further analyze the mechanism governing the Ca2+
channel-Mibefradil interaction, we examined the effect of Mibefradil on
various recombinant Ca2+ channels expressed in mammalian cells from their
cloned cDNAs, using Ca2+ as the permeant ion at physiological
concentration. Expression of alpha1A, alpha1C and alpha1E in tsA 201 cells
resulted in Ca2+ currents with functional characteristics closely related
to those of their native counterparts. Mibefradil blocked alpha1A and
alpha1E with a Kd comparable to that reported for ***T*** - ***type***
channels, but had a lower affinity (apprx30-fold) for alpha1C. For each
channel, inhibition by Mibefradil was consistent with high-affinity
binding to the inactivated state. Modulation of the voltage-dependent
inactivation properties by the nature of the coexpressed beta subunit or
the ***alpha1*** splice variant altered block at the Mibefradil
receptor site. Therefore, we conclude that the tissue and sub-cellular
localization of ***calcium*** ***channel*** subunits as well as
their specific associations are essential parameters to understand the in
vivo effects of Mibefradil.

L6 ANSWER 57 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:866265 SCISEARCH
THE GENUINE ARTICLE: 136YV
TITLE: Selective peptide antagonist of the class E
calcium ***channel*** from the venom of the
tarantula Hysterocrates gigas
AUTHOR: Newcomb R (Reprint); Szoke B; Palma A; Wang G; Chen X H;
Hopkins W; Cong R; Miller J; Urge L; TarczyHornoch K; Loo
J A; Dooley D J; Nadasdi L; Tsien R W; Lemos J; Miljanich
G
CORPORATE SOURCE: ELAN PHARMACEUT INC, 3760 HAVEN AVE, MENLO PK, CA 94025
(Reprint); UNIV MASSACHUSETTS, MED CTR, DEPT PHYSIOL,
WORCESTER, MA 01655; WARNER LAMBERT PARKE DAVIS, PARKE
DAVIS PHARMACEUT RES DIV, DEPT CHEM, ANN ARBOR, MI 48105;
WARNER LAMBERT PARKE DAVIS, PARKE DAVIS PHARMACEUT RES
DIV, DEPT NEUROSCI THERAPEUT, ANN ARBOR, MI 48105;
STANFORD UNIV, BECKMAN CTR, DEPT MOL & CELLULAR PHYSIOL,
STANFORD, CA 94305
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (3 NOV 1998) Vol. 37, No. 44, pp.
15353-15362.
Publisher: AMER CHEMICAL SOC, 1155 16TH ST, NW,
WASHINGTON, DC 20036.
ISSN: 0006-2960.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 75
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We describe the first potent and selective blocker of the class E
Ca2+-channel. SNX-482, a novel 41 amino acid peptide present in the venom
of the African tarantula, Hysterocrates gigas, was identified through its
ability to inhibit human class E Ca2+ channels stably expressed in a
mammalian cell line. An IC50 of 15-30 nM was obtained for block of the
class E Ca2+ channel, using either patch clamp electrophysiology or
K+-evoked Ca2+ flux. At low nanomolar concentrations, SNX-482 also blocked
a native resistant or R-type Ca2+ current in rat neurohypophyseal nerve
terminals, but concentrations of 200-500 nM had no effect on R-type Ca2+
cut-rents in several types of rat central neurons. The peptide has the
sequence GVDKAGCRYMFGGCSVNDDCCPRLGCHSLFSY CAWDLTFSD-OH and is homologous to
the spider peptides grammatoxin S1A and hanatoxin, both peptides with very
different ion channel blocking selectivities. No effect of SNX-482 was
observed on the following ion channel activities: Na+ or K+ currents in
several cultured cell types (up to 500 nM); K+ current through cloned
potassium channels Kv1.1 and Kv1.4 expressed in Xenopus oocytes (up to 140
nM); Ca2+ flux through L- and ***T*** - ***type*** Ca2+ channels in
an anterior pituitary cell line (GH3, up to 500 nM);

and Ba2+ current
through class A Ca2+ channels expressed in Xenopus oocytes (up to 280 nM).
A weal; effect was noted on Ca2+ current through cloned and stably
expressed class B Ca2+ channels (IC50 > 500 nM). The unique selectivity of
SNX-482 suggests its usefulness in studying the diversity, function, and
pharmacology of class E and/or R-type Ca2+ channels.

L6 ANSWER 58 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:778879 CAPLUS
DOCUMENT NUMBER: 130:107992
TITLE: Single-cell RT-PCR and functional characterization of
Ca2+ channels in motoneurons of the rat facial nucleus
AUTHOR(S): Plant, T. D.; Schirra, C.; Katz, E.; Uchitel, O. D.;
Konnerth, A.
CORPORATE SOURCE: I. Physiologisches Institut, Universitat des
Saarlandes, Homburg, 66421, Germany
SOURCE: J. Neurosci. (1998), 18(23), 9573-9584
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Voltage-dependent Ca2+ channels are a major pathway for Ca2+ entry in
neurons. We have studied the electrophysiol., pharmacol., and mol.
properties of voltage-gated Ca2+ channels in motoneurons of the rat facial
nucleus in slices of the brainstem. Most facial motoneurons express both
low voltage-activated (LVA) and high voltage-activated (HVA) Ca2+ channel
currents. The HVA current is composed of a no. of pharmacol. separable
components, including 30% of N-type and .apprx.5% of L-type. Despite the
dominating role of P-type Ca2+ channels in transmitter release at facial
motoneuron terminals described in previous studies, these channels were
not present in the cell body. Remarkably, most of the HVA current was
carried through a new type of Ca2+ channel that is resistant to toxin and
dihydropyridine block but distinct from the R-type currents described in
other neurons. Using reverse transcription followed by PCR amplification
(RT-PCR) with a powerful set of primers designed to amplify all HVA
subtypes of the . ***alpha*** . ***1*** -subunit, we identified a
highly heterogeneous expression pattern of Ca2+ channel . ***alpha*** .
1 -subunit mRNA in individual neurons consistent with the Ca2+
current components found in the cell bodies and axon terminals. We
detected mRNA for .alpha.1A in 86% of neurons, .alpha.1B in 59%, .alpha.1C
in 18%, .alpha.1D in 18%, and .alpha.1E in 59%. Either .alpha.1A or
.alpha.1B mRNAs (or both) were present in all neurons, together with
various other . ***alpha*** . ***1*** -subunit mRNAs. The most
frequently occurring combination was .alpha.1A with .alpha.1B and
.alpha.1E. Taken together, these results demonstrate that the Ca2+
channel pattern found in facial motoneurons is highly distinct from that
found in other brainstem motoneurons.
REFERENCE COUNT: 48
REFERENCE(S): (1) Bargas, J; J Neurosci 1994, V14, P6667 CAPLUS
(2) Catterall, W; Annu Rev Biochem 1995, V64, P493
CAPLUS
(3) Chin, H; Genomics 1992, V14, P1089 CAPLUS
(4) Dunlap, K; Trends Neurosci 1995, V18, P89 CAPLUS
(6) Eliot, L; J Neurophysiol 1994, V72, P762 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 59 OF 104 MEDLINE
DUPLICATE 17
ACCESSION NUMBER: 1999003395 MEDLINE
DOCUMENT NUMBER: 99003395
TITLE: Low-voltage-activated Ca2+ currents are generated by
members of the CavT subunit family (alpha1G/H) in rat
primary sensory neurons.
AUTHOR: Lambert R C; McKenna F; Maulet Y; Talley E M; Bayliss D A;
Cribbs L L; Lee J H; Perez-Reyes E; Feltz A
CORPORATE SOURCE: Laboratoire de Neurobiologie Cellulaire, UPR 9009-Centre
National de la Recherche Scientifique, F-67084, Strasbourg,
France.
CONTRACT NUMBER: HL 57828 (NHLBI)
NS 33583 (NINDS)
SOURCE: JOURNAL OF NEUROSCIENCE, (1998 Nov 1) 18 (21) 8605-13.
Journal code: JDF. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY WEEK: 19990204
AB Recently, two members of a new family of Ca2+ channel ***alpha1***
subunits, alpha1G (or CavT.1) and alpha1H (or CavT.2), have been cloned
and expressed. These ***alpha1*** subunits generate Ba2+ currents
similar to the ***T*** - ***type*** Ca2+ currents present in sensory
neurons. Here, we use three methods to investigate whether the T currents
of nodosus ganglion neurons are encoded by members of the CavT family. PCR
detected the presence of mRNA encoding both alpha1G and alpha1H, as well
as a third highly related sequence, alpha1I. In situ hybridizations
performed on nodosus ganglia demonstrate a high expression of alpha1H
subunit RNAs. Transfection of nodosus ganglion neurons with a generic
antisense oligonucleotide against this new ***alpha1*** subunit family
selectively suppresses the low-voltage-activated Ca2+ current. The
antisense oligonucleotide effect increased with time after transfection
and reached a maximum 3 d after treatment, indicating a 2-3 d turnover for
the ***alpha1*** proteins. Taken together, these results suggest that
the ***T*** - ***type*** current present in the sensory neurons is
mainly attributable to alpha1H channels. In addition, taking advantage of
the high specificity of the antisense ON to the cloned channels, we showed
that ***T*** - ***type*** currents greatly slowed the repolarization
occurring during an action potential and were responsible for up to 51% of
the Ca2+ entry during spikes. Therefore, the antisense strategy clearly
demonstrates the role of low-voltage-activated Ca2+ current in affecting
the afterpotential properties and influencing the cell excitability. Such
tools should be beneficial to further studies investigating physiological
roles of ***T*** - ***type*** Ca2+ currents.

L6 ANSWER 60 OF 104 MEDLINE
DUPLICATE 18
ACCESSION NUMBER: 1998420198 MEDLINE
DOCUMENT NUMBER: 98420198
TITLE: Mechanisms of spontaneous cytosolic Ca2+ transients in
differentiated human neuronal cells.
AUTHOR: Gao Z Y; Chen M; Collins H W; Matschinsky F M; Lee V M;
Wolf B A
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University
of Pennsylvania School of Medicine, Philadelphia 19104,
USA.
CONTRACT NUMBER: AG09215 (NIA)
AG11542 (NIA)
AG10124 (NIA)
+
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (1998 Jul) 10 (7)
2416-25.
Journal code: BYG. ISSN: 0953-816X.
PUB. COUNTRY: France
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY WEEK: 19981204
AB We have studied Ca2+ homeostasis in a unique model of human neurons, the
NT2N cell, which differentiates from a human teratocarcinoma cell line,
NTera2/C1.D1 by retinoic acid treatment. When perifused with Krebs-HEPES
buffer containing 2.5 mM CaCl2, fura-2 loaded NT2N cells produced
spontaneous cytosolic Ca2+ oscillations, or Ca2+ transients. These
cytosolic Ca2+ transients were not blocked by antagonists of glutamate
(6-cyano-7-nitroquinoxaline-2,3-dione and D(-)-2-amino-5-
phosphonopentanoic acid) or muscarinic (atropine) receptors. Omission of
extracellular Ca2+ completely abolished Ca2+ oscillations and decreased
the average Ca2+ level from 106 +/- 14 nM to 59 +/- 8 nM. Addition of the
L-type Ca2+ channel blocker nifedipine (1 or 10 microM) or of the N-type
inhibitor omega-conotoxin GVIA (5 microM) significantly, although
incompletely, suppressed Ca2+ oscillations, while omega-conotoxin MVIIC (5
microM), a selective antagonist of P- and Q-channels, had no effect. Ni2+,
at 100 microM, a concentration selective for ***T*** - ***type***
channels, did not inhibit Ca2+ transients. Non-specific blockage of Ca2+
channels by higher concentrations of Ni2+ (2-5 mM) or Co2+ (1 mM)
abolished Ca2+ oscillations completely. The endoplasmic reticulum
Ca2+-ATPase inhibitor, thapsigargin (1 microM), slightly decreased Ca2+
oscillation frequency, and induced a small transitory increase in the
average cytosolic Ca2+ concentration. The mRNAs of L- (alpha1D subunit)
and N-type (alpha1B subunit) Ca2+ channel were present in NT2N cells,
while that of a ***T*** - ***type*** Ca2+ channel (***alpha1***
-subunit) was not present in the NT2N cells as shown by reverse
transcription-polymerase chain reaction. In conclusion, NT2N neuronal
cells generate cytosolic Ca2+ oscillations mainly by influx of
extracellular Ca2+ through multiple channels, which include L- and N-type
channels, and do not require activation of glutamate or muscarinic
receptors.

L6 ANSWER 61 OF 104 MEDLINE
DUPLICATE 19
ACCESSION NUMBER: 1999055409 MEDLINE

DOCUMENT NUMBER: 99055409
TITLE: Voltage dependent ***calcium*** ***channels*** in
mammalian spermatozoa.
AUTHOR: Benoff S
CORPORATE SOURCE: Division of Human Reproduction, Department of Obstetrics
and Gynecology, North Shore University Hospital-New York
University School of Medicine, Manhasset, New York 11030,
USA.. sbenoff@nshs.edu
CONTRACT NUMBER: ES 06100 (NIEHS)
SOURCE: FRONTIERS IN BIOSCIENCE, (1998 Dec 1) 3 D1220-40. Ref: 254
Journal code: CUE. ISSN: 1093-4715.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199903
ENTRY WEEK: 19990301
AB Calcium influx is an absolute requirement for the physiological acrosome
reaction in sperm from all sources examined, both invertebrate and
mammalian. Pharmacological studies suggest that the major channel in the
sperm head plasma membrane responsible for modulating calcium entry and
intracellular ionized calcium levels could be either an L-type (a class of
high voltage-activated) or a ***T*** - ***type*** (low
voltage-activated) voltage-dependent ***calcium*** ***channel*** .
Patch clamp analysis of calcium currents in immature spermatogenic cells
demonstrates the presence of ***T*** - ***type*** currents.
Therefore, an argument has been put forth that the acrosome reaction of
ejaculated sperm is regulated by a ***T*** - ***type***
calcium ***channel*** . However, indirect analysis of calcium
currents in mature sperm after transfer of ion channels to planar lipid
bilayers detects three current types, including that similar, but not
identical, to an L-type channel, but no ***T*** - ***type***
currents. Molecular cloning of the ***alpha*** - ***1*** pore
forming subunit of ***calcium*** ***channels*** expressed in the
male reproductive tract and in ejaculated sperm has resolved this
controversy, demonstrating the existence of only high voltage-activated
channels. Further analysis of the ***alpha*** - ***1*** subunit
isoform from rat and human testis and sperm suggests that, as a result of
alternate splicing, this L-type ***alpha*** - ***1*** subunit could
produce calcium currents that were T-like, e.g., transient, rapidly
inactivating with slow deactivation. Multiple splice variants of this
isoform were detected in human testis, suggesting a correlation with
intra-individual variation in the ability of sperm to undergo an induced
acrosome reaction and with male infertility. These variants could be
developed as useful biomarkers for susceptibility to environmental and
occupational toxicants. Knowledge of ***calcium*** ***channels***
structure will also contribute to design of new male contraceptives based
on existing ***calcium*** ***channel*** antagonists.

L6 ANSWER 62 OF 104 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1998:330293 CAPLUS
DOCUMENT NUMBER: 129:63232
TITLE: Endogenous pacemaker activity of rat tumor
somatotrophs
AUTHOR(S): Kwiecien, Renata; Robert, Christophe; Cannon, Robert;
Vigues, Stephan; Arnoux, Annie; Kordon, Claude;
Hammond, Constance
CORPORATE SOURCE: Unite de Dynamique des Systemes Neuroendocriniens,
INSERM U159, Paris, 75014, Fr.
SOURCE: J. Physiol. (Cambridge, U. K.) (1998), 508(3), 883-905
CODEN: JPHYA7; ISSN: 0022-3751
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cells derived from a rat pituitary tumor (GC cell line) that continuously
release growth hormone behave as endogenous pacemakers. In simultaneous
patch clamp recordings and cytosolic Ca2+ concn. ([Ca2+]i) imaging, they
displayed rhythmic action potentials (44.7 mV, 178 ms, 0.30 Hz) and
concomitant [Ca2+]i transients (374 nM, 1.0 s, 0.27 Hz). Action
potentials and [Ca2+]i transients were reversibly blocked by removal of
external Ca2+, addn. of nifedipine (1 .mu.M) or Ni2+ (40 .mu.M), but were
insensitive to TTX (1 .mu.M). An L-type Ca2+ current activated at -33.6
mV (holding potential (Vh), -40 mV), peaked at -1.8 mV, was reduced by
nifedipine and enhanced by S-(+)-SDZ 202791. A T/R-type Ca2+ current
activated at -41.7 mV (Vh, -80 or -60 mV), peaked at -9.2 mV, was reduced
by low concns. of Ni2+ (40 .mu.M) or Cd2+ (10 .mu.M) and was
toxin-resistant. Parallel expts. revealed the expression of the class E
calcium ***channel*** . ***alpha*** . ***1*** -subunit
mRNA. The K+ channel blockers TEA (25 mM) and charybdotoxin (10-100 nM)
enhanced spike amplitude and/or duration. Apamin (100 nM) also strongly
reduced the after-spike hyperpolarization. The outward K+ tail current
evoked by a depolarizing step that mimicked an action potential reversed
at -69.8 mV, presented two components, lasted 2-3 s and was totally
blocked by Cd2+ (400 .mu.M). The slow pacemaker depolarization (3.5 s)
that sepd. consecutive spikes corresponded to a 2-3-fold increase in
membrane resistance, was strongly Na+-sensitive, but TTX-insensitive.
Computer simulations showed that pacemaker activity can be reproduced by a
min. of six currents: an L-type Ca2+ current underlies the rising phase of
action potentials that are repolarized by a delayed rectifier and
Ca2+-activated K+ currents. In between spikes, the decay of
Ca2+-activated K+ currents and a persistent inward cationic current
depolarize the membrane, activate the T/R-type Ca2+ current and initiate a
new cycle.

L6 ANSWER 63 OF 104 MEDLINE
DUPLICATE 20
ACCESSION NUMBER: 1998370780 MEDLINE
DOCUMENT NUMBER: 98370780
TITLE: Antisense depletion of beta-subunits fails to affect
T - ***type*** ***calcium*** ***channels***
properties in a neuroblastoma cell line.
AUTHOR: Leuranguer V; Bourinet E; Lory P; Nargeot J
CORPORATE SOURCE: Institut de Genetique Humaine (UPR 1142), Montpellier,
France.
SOURCE: NEUROPHARMACOLOGY, (1998 Jun) 37 (6) 701-8.
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104
AB Voltage-gated ***calcium*** ***channels*** can be classified into
high voltage activated (HVA) and low voltage activated (LVA or ***T***
- ***type***) subtypes. The molecular diversity of HVA channels
primarily results from different genes encoding their pore-forming
alpha1 subunits. These channels share a common structure with an
alpha1 subunit associated with at least two regulatory subunits
(beta, alpha2-delta). Any of the six ***alpha1*** -related channels
identified to date are regulated in their functional properties through an
interaction with the ancillary beta-subunit. By contrast, the diversity
and the molecular identity of LVA or ***T*** - ***type***
calcium ***channels*** have yet to be defined. Whether LVA
channels are modulated by a beta-subunit, like HVA channels, is unknown.
To address this issue, we have used an antisense strategy to inhibit
beta-subunit expression in the NG 108-15 neuroblastoma cell line.
Differentiated NG 108-15 cells express both LVA and HVA channels. We found
that LVA currents were unaffected when cells were incubated with
beta-antisense, while HVA currents were drastically decreased. Since LVA
Ca channel currents in NG 108-15 cells are not regulated by beta-subunits,
it is reasonable to postulate that the pore-forming subunit(s) of these
channels lacks an interaction domain with a beta-subunit (AID). This
molecular feature, which is common to various ***T*** - ***type***
channels, indicates further that LVA ***calcium*** ***channels***
belong to a channel family structurally distant from HVA channels.

L6 ANSWER 64 OF 104 MEDLINE
DUPLICATE 21
ACCESSION NUMBER: 1998355943 MEDLINE
DOCUMENT NUMBER: 98355943
TITLE: Electrophysiological properties of neonatal rat ventricular
myocytes with ***alpha1*** -adrenergic-induced
hypertrophy.
AUTHOR: Gaughan J P; Hefner C A; Houser S R
CORPORATE SOURCE: Department of Physiology, Temple University School of
Medicine, Philadelphia, Pennsylvania 19140, USA.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1998 Aug) 275 (2 Pt 2) H577-90.
Journal code: 3U8. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199811
AB The electrophysiology of neonatal rat ventricular myocytes with and
without hypertrophy has not been characterized. The ***alpha1***
-adrenergic agonist phenylephrine induced hypertrophy in neonatal rat
ventricular myocytes. After 48 h of exposure to 20

microM phenylephrine,
cell surface area of hypertrophied myocytes was 44% larger than control.
Action potential duration was significantly longer in hypertrophy than in
control. There was an increase in L-type Ca2+ current in control after 48
h in culture, but current density was significantly less in hypertrophy
(-4.7 +/- 0.8 hypertrophy vs. -10.7 +/- 1.2 control pA/pF, n = 22, P <
0.05). ***T*** - ***type*** Ca2+ current density was not different.
The alpha-adrenergic antagonist prazosin blocked the hypertrophy and the
chronic effect of phenylephrine on L-type Ca2+ current. Transient outward
K+ current density was decreased 70% in hypertrophy and was blocked with
4-aminopyridine. No change in Na+ current density was observed.
Staurosporine, a protein kinase C inhibitor, eliminated the hypertrophy
and the effect on L-type Ca2+ current. These studies showed that
phenylephrine-induced hypertrophy occurred via the ***alpha1***
-adrenergic pathway and caused electrophysiological changes and effects on
ion channel expression.

L6 ANSWER 65 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:8432 BIOSIS
DOCUMENT NUMBER: PREV199900008432
TITLE: Low-voltage-activated (***T*** - ***type***)
calcium - ***channel*** genes identified.
AUTHOR(S): Huguenard, John R. (1)
CORPORATE SOURCE: (1) Dep. Neurol. Neurol. Sci., Stanford Univ. Sch. Med.,
Stanford, CA 94305-5122 USA
SOURCE: Trends in Neurosciences, (Nov., 1998) Vol. 21, No. 11, pp.
451-452.
ISSN: 0166-2236.
DOCUMENT TYPE: Article
LANGUAGE: English

L6 ANSWER 66 OF 104 MEDLINE
DUPLICATE 22
ACCESSION NUMBER: 1998384559 MEDLINE
DOCUMENT NUMBER: 98384559
TITLE: The effect of overexpression of auxiliary Ca2+ channel
subunits on native Ca2+ channel currents in undifferentiated mammalian NG108-15 cells.
AUTHOR: Wyatt C N; Page K M; Berrow N S; Brice N L; Dolphin A C
CORPORATE SOURCE: Department of Pharmacology, University College London, UK.
SOURCE: JOURNAL OF PHYSIOLOGY, (1998 Jul 15) 510 (Pt 2) 347-60.
Journal code: JQV. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104
AB 1. High voltage activated (HVA) Ca2+ channels are composed of a
pore-forming ***alpha*** ***1*** subunit and the accessory beta
and alpha2-delta subunits. However, the subunit composition of low voltage
activated (LVA), or ***T*** - ***type*** , Ca2+ channels has yet to
be elucidated. We have examined whether native ***calcium***
channels in NG108-15 mouse neuroblastoma x rat glioma hybrid
cells, which express predominantly LVA currents when undifferentiated, are
modulated by overexpression of accessory ***calcium*** ***channel***
subunits. 2. Endogenous alpha 1A, B, C, C, and E, and low levels of beta
and alpha 2-delta subunit protein were demonstrated in undifferentiated
NG108-15 cells. 3. The alpha 2-delta, beta 2a or beta 1b accessory
subunits were overexpressed by transfection of the cDNAs into these cells,
and the effect examined on the endogenous Ca2+ channel currents.
Heterologous expression, particularly of alpha 2-delta but also of beta 2a
subunits clearly affected the profile of these currents. Both subunits
induced a sustained component in the currents evoked by depolarizing
voltages above -30 mV, and alpha 2-delta additionally caused a
depolarization in the voltage dependence of current activation, suggesting
that it also affected the native ***T*** - ***type*** currents. In
contrast, beta 1b overexpression had no effect on the endogenous Ca2+
currents, despite immunocytochemical evidence for its expression in the
transfected cells. 4 These results suggest that in NG108-15 cells,
overexpression of the Ca2+ channel accessory subunits alpha 2-delta and
beta 2a induce a sustained component of HVA current, and alpha 2-delta
also influences the voltage dependence of activation of the LVA current.
It is possible that native ***T*** - ***type*** ***alpha***
1 subunits are not associated with beta subunits.

L6 ANSWER 67 OF 104 MEDLINE
DUPLICATE 23
ACCESSION NUMBER: 1998150958 MEDLINE
DOCUMENT NUMBER: 98150958
TITLE: Known ***calcium*** ***channel*** ***alpha1***
subunits can form low threshold small conductance channels
with similarities to native ***T*** - ***type***
channels.
AUTHOR: Meir A; Dolphin A C
CORPORATE SOURCE: Department of Pharmacology, University College London, United Kingdom.
SOURCE: NEURON, (1998 Feb) 20 (2) 341-51.
Journal code: AN8. ISSN: 0896-6273.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY WEEK: 19980503
AB Native ***T*** - ***type*** voltage-dependent ***calcium***
channels are low voltage-activated and have a small single channel
conductance of 5-8 pS, which distinguishes them from any known cloned
calcium ***channels*** whose conductances are 12-25 pS. Here,
we show that when alpha1B, alpha1E, or alpha1C are expressed in COS7
cells, which contain no endogenous ***calcium*** ***channel***
subunits or ***calcium*** ***channels*** , they each exhibit a 4-7
pS channel as well as a large conductance channel. At low depolarizations,
or when the ***alpha1*** subunit is expressed in the absence of
auxiliary alpha2-delta or beta subunits, the small conductance channels
are seen alone, and their biophysical properties, including voltage
dependence and kinetics of activation and inactivation, are very similar
to native ***T*** - ***type*** ***calcium*** ***channels*** .

L6 ANSWER 68 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:479530 BIOSIS
DOCUMENT NUMBER: PREV199800479530
TITLE: Molecular characterization of a novel family of low
voltage-activated, ***T*** - ***type*** ,
calcium ***channels*** .
AUTHOR(S): Perez-Reyes, Edward (1)
CORPORATE SOURCE: (1) Dep. Physiol., Cardiovasc. Inst., Loyola Univ. Med.
Cent., Maywood, IL 60153 USA
SOURCE: Journal of Bioenergetics and Biomembranes, (Aug., 1998)
Vol. 30, No. 4, pp. 313-318.
ISSN: 0145-479X.
DOCUMENT TYPE: General Review
LANGUAGE: English
AB Low voltage-activated, ***T*** - ***type*** , ***calcium***
channels are thought to be involved in pacemaker activity, low
threshold Ca2+ spikes, neuronal oscillations and resonance, and rebound
burst firing. Mutations in ***T*** - ***type*** channel genes may be
a contributing factor to neurological and cardiovascular disorders, such
as epilepsy, arrhythmia, and hypertension. Due to the lack of selective
blockers, little is known about their structure or molecular biology. This
review discusses our recent findings on the cloning, chromosomal
localization, and functional expression, of two novel channels, alpha1G
and alpha1H. The biophysical properties of these cloned channels
(distinctive voltage dependence, kinetics, and single channel conductance)
demonstrates that these channels are members of the ***T*** -
type Ca2+ channel family.

L6 ANSWER 69 OF 104 MEDLINE
DUPLICATE 24
ACCESSION NUMBER: 1999191101 MEDLINE
DOCUMENT NUMBER: 99191101
TITLE: Structure and function of neuronal Ca2+ channels and their
role in neurotransmitter release.
AUTHOR: Catterall W A
CORPORATE SOURCE: Department of Pharmacology, University of Washington, Seattle 98195-7280, USA.
SOURCE: CELL CALCIUM, (1998 Nov-Dec) 24 (5-6) 307-23. Ref: 151
Journal code: CQE. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY WEEK: 19990801
AB Electrophysiological studies of neurons reveal different Ca2+ currents
designated L-, N-, P-, Q-, R-, and ***T*** - ***type*** .
High-voltage-activated neuronal Ca2+ channels are complexes of a
pore-forming ***alpha*** ***1*** subunit of about 190-250 kDa, a
transmembrane, disulfide-linked complex of alpha 2 and delta subunits, and
an intracellular beta subunit, similar to the ***alpha*** ***1*** ,
alpha 2 delta, and beta subunits previously described for skeletal muscle
Ca2+ channels. The primary structures of these subunits have all been
determined by homology cDNA cloning using the corresponding subunits of
skeletal muscle Ca2+ channels as probes. In most neurons, L-type channels
contain alpha 1C or alpha 1D subunits, N-type contain alpha 1B subunits,

P- and Q-types contain alternatively spliced forms of alpha 1A subunits,
R-type contain alpha 1E subunits, and ***T*** - ***type*** contain
alpha 1G or alpha 1H subunits. Association with different beta subunits
also influences Ca2+ channel gating substantially, yielding a remarkable
diversity of functionally distinct molecular species of Ca2+ channels in
neurons.

L6 ANSWER 70 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:359279 CAPLUS
DOCUMENT NUMBER: 129:120585
TITLE: Does .alpha.1E code for ***T*** - ***type*** ***calcium*** ***channels*** ? A comparison of
recombinant .alpha.1E ***calcium*** ***channels*** with GH3 pituitary ***T*** -
type and recombinant .alpha.1B ***calcium*** ***channels***
AUTHOR(S): Rock, David M.; Horne, William A.; Stoehr, Sally J.;
Hashimoto, Chica; Zhou, Mei; Cong, Ruth; Palma,
Andrew; Hidayetoglu, Debra; Offord, James
CORPORATE SOURCE: Neuroscience Therapeutics, Parke-Davis Pharmaceutical
Research Division, Warner-Lambert Company, Ann Arbor,
MI, USA
SOURCE: Low-Voltage-Act. T-type Calcium Channels, Proc. Int.
Electrophysiol. Meet. (1998), Meeting Date 1996,
279-289. Editor(s): Tsien, Richard W.; Clozel,
Jean-Paul; Nargeot, Joel. Adis International Ltd.:
Chester, UK.
CODEN: 66EIAQ
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Expression of .alpha.1E (E class) subunits in Xenopus oocytes or in
mammalian cell lines produces ***calcium*** ***channels*** that
show rapid inactivation. It was originally proposed that .alpha.1E was
the . ***alpha*** . ***1*** subunit for low-voltage-activated (LVA)
calcium ***channels*** . Under identical recording conditions,
the authors compared biophys. and pharmacol. properties of .alpha.1E
expressed in HEK293 cells with .alpha.1B (B class) expressed in the same
cell line and LVA ***calcium*** ***channel*** currents in a rat
pituitary cell line (GH3). .alpha.1E ***Calcium*** ***channels***
showed biophys. properties that were similar to those of .alpha.1B
channels, activation voltages that were depolarized relative to GH3
T - ***type*** current and potent block by Ca12+ and the
non-selective ***calcium*** ***channel*** toxin .omega.-Aga-IIIA.
These features of .alpha.1E ***calcium*** ***channels*** are
similar to those of R-type ***calcium*** ***channels*** described
in cerebellar granule neurons, and not to GH3 ***T*** - ***type***
or other LVA ***calcium*** ***channels*** .

L6 ANSWER 71 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:781737 SCISEARCH
THE GENUINE ARTICLE: 125MZ
TITLE: New isoform of the neuronal Ca2+ channel alpha 1E subunit
in islets of Langerhans and kidney - Distribution of
voltage-gated Ca2+ channel ***alpha*** ***1***
subunits in cell lines and tissues
AUTHOR: Vajna R; Schramm M; Pereverzev A; Arnhold S; Grabsch H;
Klockner U; PerezReyes E; Hescheler J; Schneider T
(Reprint)
CORPORATE SOURCE: UNIV COLOGNE, INST NEUROPHYSIOL, ROBERT KOCH STR 39,
D-50931 COLOGNE, GERMANY (Reprint); UNIV COLOGNE, INST
NEUROPHYSIOL, D-50931 COLOGNE, GERMANY; UNIV COLOGNE, INST
ANAT 1, D-5000 COLOGNE, GERMANY; KLINIKUM LEVERKUSEN, INST
PATHOL, LEVERKUSEN, GERMANY; UNIV COLOGNE, INST VET
PHYSIOL, COLOGNE, GERMANY; LOYOLA UNIV, MED CTR,
CARDIOVASC INST, CHICAGO, IL; LOYOLA UNIV, MED CTR, DEPT
PHYSIOL, CHICAGO, IL
COUNTRY OF AUTHOR: GERMANY; USA
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (OCT 1998) Vol. 257, No.
1, pp. 274-285.
Publisher: SPRINGER VERLAG, 175 FIFTH AVE, NEW YORK, NY
10010.
ISSN: 0014-2956.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 57
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The expression of Ca2+ channel alpha 1E isoforms has been analyzed in
different cell lines, embryoid bodies and tissues. The comparison of the
different cloned alpha 1E cDNA sequences led to the prediction of alpha 1E
splice variants. Transcripts of two cloned alpha 1E isoforms, which are
discriminated by a carboxy terminal 129-bp sequence, have been detected in
different cell lines and tissues. Transcripts of the shorter alpha 1E
isoform have been assigned to the rat cerebrum and to neuron-like cells
from in vitro. differentiated embryonic stem cells. The shorter isoform is
the major transcript amplified from total RNA by reverse transcription
(RT)-PCR and visualized on the protein level by Western blotting with
common and isoform-specific antibodies. Transcripts of the longer alpha 1E
isoform have been identified in mouse, rat and human cerebellum. in in
vitro. differentiated embryoid bodies, in the insulinoma cell lines INS-1
(rat) and beta TC-3 (mouse). in the pituitary cell line AtT-20 (mouse)
when grown in 5 mM glucose, and in islets of Langerhans (rat) and kidney
(rat and human). The detection of different-isoforms of alpha 1E in cell
lines and tissues shows that the wide expression of alpha 1E has to be
specified by identifying the corresponding isoforms in each tissue. In
islets of Langerhans and in kidney, a distinct isoform called alpha 1Ee
has been determined by RT-PCR, while in cerebellum a set of different
alpha 1E structures has been detected. which might reflect the functional
heterogeneity of cerebellar neurons. The tissue-specific expression of
different isoforms might be related to specific functions. which are not
yet known, but the expression of the new isoform alpha 1Ee in islets of
Langerhans and kidney leads to the suggestion that alpha 1E might be
involved in the modulation of the Ca2+-mediated hormone secretion.

L6 ANSWER 72 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:359266 CAPLUS
DOCUMENT NUMBER: 129:133906
TITLE: Localization and function of brain ***calcium***
channels
AUTHOR(S): Catterall, William A.; Westenbroek, Ruth E.; Herlitze,
Stefan; Yokoyama, Charles T.
CORPORATE SOURCE: Department of Pharmacology, University of Washington,
Seattle, WA, USA
SOURCE: Low-Voltage-Act. T-type Calcium Channels, Proc. Int.
Electrophysiol. Meet. (1998), Meeting Date 1996,
207-217. Editor(s): Tsien, Richard W.; Clozel,
Jean-Paul; Nargeot, Joel. Adis International Ltd.:
Chester, UK.
CODEN: 66EIAQ
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 43 refs. Ca2+ channels in the brain are complexes
consisting of an . ***alpha*** . ***1*** subunit (190-250 kDa),
.alpha.2.delta. subunits (disulfide-linked dimers of 140 and 27 kDa), and
a .beta. subunit (55-72 kDa). The different physiol. and pharmacol.
properties of the various Ca2+ channel subtypes (L, N, P, Q, R, and
T ***types***) are thought to be detd. by their . ***alpha***
. ***1*** subunits. Five distinct . ***alpha*** . ***1***
subunits, designated .alpha.1A to .alpha.1E are expressed in brain. Here,
research from the authors' lab. focusing on the biochem. properties,
subcellular localization, and functional specialization of these related
neuronal . ***alpha*** . ***1*** subunits are discussed.

L6 ANSWER 73 OF 104 MEDLINE DUPLICATE 25
ACCESSION NUMBER: 1998171311 MEDLINE
DOCUMENT NUMBER: 98171311
TITLE: Calcium currents and transients of native and
heterologously expressed mutant skeletal muscle DHP
receptor ***alpha1*** subunits (R528H).
AUTHOR: Jurkat-Rott K; Uetz U; Pika-Hartlaub U; Powell J; Fontaine
B; Melzer W; Lehmann-Horn F
CORPORATE SOURCE: Abteilung fur Angewandte Physiologie, Universitat Ulm,
Germany.
SOURCE: FEBS LETTERS, (1998 Feb 20) 423 (2) 198-204.
Journal code: EUH. ISSN: 0014-5793.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199806
AB Rabbit cDNA of the ***alpha1*** subunit of the skeletal muscle
dihydropyridine (DHP) receptor was functionally expressed in a muscular
dysgenesis mouse (mdg) cell line, GLT. L-type calcium currents and
transients were recorded for the wild type and a mutant ***alpha1***
subunit carrying an R528H substitution in the supposed voltage sensor of
the second channel domain that is linked to a human

disease, hypokalemic
periodic paralysis. L-type channels expressed in GLT myotubes exhibited
currents similar to those described for primary cultured mdg cells
injected with rabbit wild type cDNA, indicating this system to be useful
for functional studies of heterologous DHP receptors. Voltage dependence
and kinetics of activation and inactivation of L-type calcium currents
from mutant and wild type channels did not differ significantly.
Intracellular calcium release activation measured by fura-2
microfluorimetry was not grossly altered by the mutation either. Analogous
measurements on myotubes of three human R528H carriers revealed calcium
transients comparable to controls while the voltage dependence of both
activation and inactivation of the L-type current showed a shift to more
negative potentials of approximately 6 mV. Similar effects on the voltage
dependence of the fast ***T*** - ***type*** current and changes in
the expression level of the third-type calcium current point to factors
not primarily associated with the mutation perhaps participating in
disease pathogenesis.

L6 ANSWER 74 OF 104 MEDLINE
DUPLICATE 26
ACCESSION NUMBER: 1998333998 MEDLINE
DOCUMENT NUMBER: 98333998
TITLE: Cloning and characterization of alpha1H from human heart, a
member of the ***T*** - ***type*** Ca2+ channel gene
family.
AUTHOR: Cribbs L L; Lee J H; Yang J; Satin J; Zhang Y; Daud A;
Barclay J; Williamson M P; Fox M; Rees M; Perez-Reyes E
CORPORATE SOURCE: Department of Physiology, Cardiovascular Institute, Loyola
University Medical Center, Maywood, Ill 60153, USA..
lcribbs@luc.edu
SOURCE: CIRCULATION RESEARCH, (1998 Jul 13) 83 (1) 103-9.
Journal code: DAJ. ISSN: 0009-7330.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF051946; GENBANK-AF051947
ENTRY MONTH: 199810
AB Voltage-activated Ca2+ channels exist as multigene families that share
common structural features. Different Ca2+ channels are distinguished by
their electrophysiology and pharmacology and can be classified as either
low or high voltage-activated channels. Six ***alpha1*** subunit genes
cloned previously code for high voltage-activated Ca2+ channels;
therefore, we have used a database search strategy to identify new Ca2+
channel genes, possibly including low voltage-activated (***T*** -
type) channels. A novel expressed sequence-tagged cDNA clone of
alpha1G was used to screen a cDNA library, and in the present study, we
report the cloning of alpha1H (or CavT.2), a low voltage-activated Ca2+
channel from human heart. Northern blots of human mRNA detected more
alpha1H expression in peripheral tissues, such as kidney and heart, than
in brain. We mapped the gene, CACNA1H, to human chromosome 16p13.3 and
mouse chromosome 17. Expression of alpha1H in HEK-293 cells resulted in
Ca2+ channel currents displaying voltage dependence, kinetics, and unitary
conductance characteristic of native ***T*** - ***type*** Ca2+
channels. The alpha1H channel is sensitive to mibefradil, a
nondihydropyridine Ca2+ channel blocker, with an IC50 of 1.4 micromol/L,
consistent with the reported potency of mibefradil for ***T*** -
type Ca2+ channels. Together with alpha1G, a rat brain ***T***
- ***type*** Ca2+ channel also cloned in our laboratory, these genes
define a unique family of Ca2+ channels.

L6 ANSWER 75 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:293627 BIOSIS
DOCUMENT NUMBER: PREV199800293627
TITLE: Single channel mechanism of mibefradil action on
alpha1E-and ***T*** - ***type*** ***calcium***
channels .
AUTHOR(S): Handrock, R. (1); Schroeder, F. (1); Demirel-Yilmaz, E.;
Kreuzberg, U. (1); Pereverzev, A.; Schneider, T.; Herzig,
S. (1)
CORPORATE SOURCE: (1) Dep. Pharmacol., Gleueler Str. 24, 50931 Cologne
Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (1998) Vol.
357, No. 4 SUPPL, pp. R70.
Meeting Info.: 39th Spring Meeting of the German Society
for Experimental and Clinical Pharmacology and Toxicology
Mainz, Germany March 17-19, 1998 German Society for
Experimental and Clinical Pharmacology and Toxicology
. ISSN: 0028-1298.
DOCUMENT TYPE: Conference
LANGUAGE: English

L6 ANSWER 76 OF 104 MEDLINE
DUPLICATE 27
ACCESSION NUMBER: 1998231527 MEDLINE
DOCUMENT NUMBER: 98231527
TITLE: Voltage dependent ***calcium*** ***channels*** in
adrenal glomerulosa cells and in insulin producing cells.
AUTHOR: Horvath A; Szabadkai G; Varnai P; Aranyi T; Wollheim C B;
Spat A; Enyedi P
CORPORATE SOURCE: Department of Physiology and Laboratory of Cellular and
Molecular Physiology, Semmelweis University of Medicine,
Budapest, Hungary.
SOURCE: CELL CALCIUM, (1998 Jan) 23 (1) 33-42.
Journal code: CQE. ISSN: 0143-4160.
PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
AB We have examined the structure and function of Ca2+ channels in excitable
endocrine cell types, in rat adrenal glomerulosa cells and in two insulin
producing cell types, the rat pancreatic beta cell and the INS-1 cell
line. In previous studies on glomerulosa cells, we observed low (***T***
- ***type***) and high threshold (L-type) voltage dependent Ca2+
currents in addition to a K+ induced inward rectifying Ca2+ current (Igl).
beta cells are known to exhibit T-, L- and N-type currents. We have now
found that INS-1 cells also show low threshold (***T*** - ***type***
) and high threshold Ca2+ currents. The latter was further resolved by
organic inhibitors into L-type and P/Q-type currents and no Igl was
detected. The expression of the pore-forming ***alpha*** ***1***
subunit of voltage dependent Ca2+ channels was studied by means of reverse
transcription-polymerase chain reaction (RT-PCR), followed by restriction
enzyme mapping and/or sequencing. Both in glomerulosa and pancreatic beta
cells, the neuroendocrine (D) class of the ***alpha*** ***1***
subunit, known to be responsible for L-type current, represents the
majority of the PCR product. Comparable amounts of the neuroendocrine (D)
and the neuronal A-type ***alpha*** ***1*** subunits dominate the
message in INS-1 cells. Different characteristics of Ca2+ currents in
these cell types is discussed in view of the channel repertoire.

L6 ANSWER 77 OF 104 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1999:53497 BIOSIS
DOCUMENT NUMBER: PREV199900053497
TITLE: The safety of ***calcium*** - ***channel*** blockers.
AUTHOR(S): Massie, Barry M. (1)
CORPORATE SOURCE: (1) Univ. Calif. San Francisco, Cardiol. Div., VA Hosp.,
4150 Clement Street, San Francisco, CA 94121 USA
SOURCE: Clinical Cardiology, (Dec., 1998) Vol. 21, No. 12 SUPPL. 2,
pp. II12-II17.
ISSN: 0160-9289.
DOCUMENT TYPE: Article
LANGUAGE: English
AB ***Calcium*** - ***channel*** blockers are widely used as an
effective treatment for hypertension and angina. Several studies have
raised questions about their safety, suggesting that ***calcium*** -
channel blockers can increase the rates of myocardial infarction
(MI) and death, particularly in patients with heart disease. Reviews of
these studies have uncovered serious methodological shortcomings or have
found them restricted to short-acting drugs, frequently at high doses or
used inappropriately. One study was based on old data regarding only
short-acting nifedipine, which has never been indicated for patients who
have suffered an MI or unstable angina. A case-control study of
short-acting verapamil, diltiazem, and nifedipine suggested an increased
MI rate was confounded by the higher rates of diabetes and preexisting
heart disease in the patients treated with ***calcium*** -
channel blockers. A third study reported significantly decreased
survival only in patients taking short-acting nifedipine; in most of the
cases reported, blood pressure was not controlled. While these studies
alert us to the limitations of short-acting ***calcium*** -
channel blockers and the necessity of considering side effects
such as neurohormonal stimulation, a number of more recent,
better-controlled studies have not confirmed increased risk with
calcium - ***channel*** blockers when appropriately employed.
Calcium - ***channel*** blockers should still be considered
first-line therapy in appropriately selected patients with hypertension or
angina.

L6 ANSWER 78 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:49547 SCISEARCH
THE GENUINE ARTICLE: YN574
TITLE: Antisense oligonucleotides against rat brain alpha(1E) DNA
and its atrial homologue decrease ***T*** - ***type*** calcium current in atrial myocytes
AUTHOR: PiedrasRenteria E S; Chen C C; Best P M (Reprint)
CORPORATE SOURCE: 524 BURRILL HALL, MC-114, 407 S GOODWIN AVE, URBANA, IL 61801 (Reprint); UNIV ILLINOIS, DEPT MOL & INTEGRAT PHYSIOL, URBANA, IL 61801; UNIV ILLINOIS, COLL MED, URBANA, IL 61801
COUNTRY OF AUTHOR: USA
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (23 DEC 1997) Vol. 94, No. 26, pp. 14936-14941.
Publisher: NATL ACAD SCIENCES, 2101 CONSTITUTION AVE NW, WASHINGTON, DC 20418.
ISSN: 0027-8424.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Low voltage-activated, or ***T*** - ***type*** , calcium currents
are important regulators of neuronal and muscle excitability, secretion,
and possibly cell growth and differentiation, The gene (or genes) coding
for the pore-forming subunit of low voltage-activated channel proteins has
not been unequivocally identified. We have used reverse transcription-PCR
to identify partial clones from rat atrial myocytes that share high
homology with a member of the E class of ***calcium*** ***channel*** genes, Antisense oligonucleotides targeting one of these partial clones
(raE1) specifically block the increase in T-current density that normally
results when atrial myocytes are treated with insulin-like growth factor I
(IGF-1), Antisense oligonucleotides targeting portions of the neuronal rat
alpha(1E) sequence, which are not part of the clones detected in atrial
tissue, also block the IGF-l-induced increase in T-current, suggesting
that the high homology to alpha(1E) seen in the partial clone may be
present in the complete atrial sequence. The basal T-current expressed in
these cells is also blocked by antisense oligonucleotides, which is
consistent with the notion that IGF-1 up-regulates the same gene that
encodes the basal current, These results support the hypothesis that a
member of the E class of ***calcium*** ***channel*** genes encodes
a low voltage-activated ***calcium*** ***channel*** in atrial
myocytes.

L6 ANSWER 79 OF 104 MEDLINE
DUPLICATE 28
ACCESSION NUMBER: 97402507 MEDLINE
DOCUMENT NUMBER: 97402507
TITLE: ***T*** - ***type*** Ca2+ current properties are not
modified by Ca2+ channel beta subunit depletion in nodosus ganglion neurons.
AUTHOR: Lambert R C; Maulet Y; Mouton J; Beattie R; Volsen S; De
Waard M; Feltz A
CORPORATE SOURCE: Laboratoire de Neurobiologie Cellulaire, UPR 9009 Centre National de la Recherche Scientifique, 67084 Strasbourg, France.
SOURCE: JOURNAL OF NEUROSCIENCE, (1997 Sep 1) 17 (17) 6621-8.
Journal code: JDF. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971104
AB At the molecular level, our knowledge of the low voltage-activated Ca2+
channel (***T*** - ***type***) has made little progress. Using an
antisense strategy, we investigated the possibility that the ***T*** -
type channels have a structure similar to high voltage-activated
Ca2+ channels. It is assumed that high voltage-activated channels are made
of at least three components: a pore forming ***alpha1*** subunit
combined with a cytoplasmic modulatory beta subunit and a primarily
extracellular alpha2delta subunit. We have examined the effect of
transfecting cranial primary sensory neurons with generic anti-beta
antisense oligonucleotides. We show that in this cell type, blocking
expression of all known beta gene products does not affect ***T*** -
type current, although it greatly decreases the current amplitude
of high voltage-activated channels and modifies their voltage dependence.
This suggests that beta subunits are likely not constitutive of ***T***
- ***type*** Ca2+ channels in this cell type.

L6 ANSWER 80 OF 104 MEDLINE
DUPLICATE 29
ACCESSION NUMBER: 97383272 MEDLINE
DOCUMENT NUMBER: 97383272
TITLE: Differential localization of voltage-dependent
calcium ***channel*** ***alpha1*** subunits
at the human and rat neuromuscular junction.
AUTHOR: Day N C; Wood S J; Ince P G; Volsen S G; Smith W; Slater C
R; Shaw P J
CORPORATE SOURCE: MRC Neurochemical Pathology Unit, Newcastle General Hospital, Newcastle upon Tyne NE4 6BE, United Kingdom.
SOURCE: JOURNAL OF NEUROSCIENCE, (1997 Aug 15) 17 (16) 6226-35.
Journal code: JDF. ISSN: 0270-6474.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199710
ENTRY WEEK: 19971005
AB Neurotransmitter release is regulated by voltage-dependent ***calcium***
channels (VDCCs) at synapses throughout the nervous system. At the
neuromuscular junction (NMJ) electrophysiological and pharmacological
studies have identified a major role for P- and/or Q-type VDCCs in
controlling acetylcholine release from the nerve terminal. Additional
studies have suggested that N-type channels may be involved in
neuromuscular transmission. VDCCs consist of pore-forming ***alpha1***
and regulatory beta subunits. In this report, using fluorescence
immunocytochemistry, we provide evidence that immunoreactivity to alpha1A,
alpha1B, and alpha1E subunits is present at both rat and human adult NMJs.
Using control and denervated rat preparations, we have been able to
establish that the subunit thought to correspond to P/Q-type channels,
alpha1A, is localized presynaptically in discrete puncta that may
represent motor nerve terminals. We also demonstrate for the first time
that alpha1A and alpha1B (which corresponds to N-type channels) may be
localized in axon-associated Schwann cells and, further, that the alpha1B
subunit may be present in perisynaptic Schwann cells. In addition, the
alpha1E subunit (which may correspond to R/ ***T*** - ***type*** channels) seems to be localized postsynaptically in the muscle fiber
membrane and concentrated at the NMJ. The possibility that all three VDCCs
at the NMJ are potential targets for circulating autoantibodies in
amyotrophic lateral sclerosis is discussed.

L6 ANSWER 81 OF 104 SCISEARCH
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ACCESSION NUMBER: 1998:79084 SCISEARCH
THE GENUINE ARTICLE: YR308
TITLE: Voltage-dependent Ca2+ channels in arterial smooth muscle
cells
AUTHOR: Gollasch M (Reprint); Nelson M T
CORPORATE SOURCE: HUMBOLDT UNIV BERLIN, FRANZ VOLHARD CLIN, WILTBERGSTR 50, D-13125 BERLIN, GERMANY (Reprint); UNIV VERMONT, DEPT PHARMACOL, MED RES FACIL, COLCHESTER, VT
COUNTRY OF AUTHOR: GERMANY; USA
SOURCE: KIDNEY & BLOOD PRESSURE RESEARCH, (DEC 1997) Vol. 20, No. 6, pp. 355-371.
Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
ISSN: 1420-4096.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 222
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The past years have seen some significant advances in our understanding
of the functional and molecular properties of voltage-dependent Ca2+
channels in arterial smooth muscle. Molecular cloning and expression
studies together with experiments on native voltage-dependent Ca2+
channels revealed that these channels are built upon a molecular structure
with properties appropriate to function as the main source for Ca2+ entry
into arterial smooth muscle cells. This Ca2+ entry regulates intracellular
free Ca2+, and thereby arterial tone. We summarize several avenues of
recent research that should provide significant insights into the
functioning of voltage-dependent Ca2+ channels under conditions that occur
in arterial smooth muscle. These experiments have identified important
features of voltage-dependent Ca2+ channels, including the steep
steady-state voltage-dependence of the channel open probability at steady
physiological membrane potentials between -60 and -30 mV, and a relatively
high permeation rate at physiological Ca2+ concentrations, being about one
million Ca2+ ions/s at -50 mV. This calcium permeation rate seems to be a
feature of the pore-forming Ca2+ channel ***alpha*** (***1***)
subunit, since it was identical for native channels and the expressed

alpha (***1***) subunit alone. The channel activity is regulated by dihydropyridines, vasoactive hormones and intracellular signaling pathways. While the membrane potential of smooth muscle cells primarily regulates arterial muscle tone through alterations in Ca2+ influx through dihydropyridine-sensitive voltage-dependent ('L-type') Ca2+ channels, the role of these channels in the differentiation and proliferation of vascular smooth muscle cells is less clear. We discuss recent findings suggesting that other Ca2+ permeable ion channels might be important for the control of Ca2+ influx in dedifferentiated vascular smooth muscle cells.

L6 ANSWER 82 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)DUPLICATE 30
ACCESSION NUMBER: 97:586711 SCISEARCH
THE GENUINE ARTICLE: XN392
TITLE: Toxin-resistant calcium currents, in embryonic mouse sensory neurons
AUTHOR: Hilaire C; Diochot S; Desmadryl G (Reprint); Richard S; Valmier J
CORPORATE SOURCE: INST BIOL, CNRS, UPR 9008, LAB MED EXPTL, INSERM, U249, BLVD HENRI IV, F-34060 MONTPELLIER, FRANCE (Reprint); INST BIOL, CNRS, UPR 9008, LAB MED EXPTL, INSERM, U249, F-34060 MONTPELLIER, FRANCE; UNIV MONTPELLIER 2, INSERM, U432, F-34095 MONTPELLIER 5, FRANCE; CNRS, CRBM, UPR 9008, INSERM, U249, F-34033 MONTPELLIER, FRANCE
COUNTRY OF AUTHOR: FRANCE
SOURCE: NEUROSCIENCE, (SEP 1997) Vol. 80, No. 1, pp. 267-276. Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD, ENGLAND OX5 1GB. ISSN: 0306-4522.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB We characterized toxin-insensitive calcium currents expressed by acutely dissociated embryonic dorsal root ganglion neurons. In the presence of 3 mu M omega-conotoxin-GVIA, 3 mu M nitrendipine and either 500 nM omega-agatoxin-IVA or 500 nM omega-conotoxin-MVIIC to inhibit N-, L- and P/Q-type currents, respectively, all neurons expressed two residual currents: a ***T*** - ***type*** and another which we referred to as toxin-resistant current. The toxin-resistant current (i) consisted of an inactivating and a sustained components, (ii) had a threshold of activation and a steady-state inactivation comprised between that of the ***T*** - ***type*** current and that of the other high-voltage-activated currents, (iii) had the same permeability for barium and calcium used as charge carriers, (iv) was highly sensitive to both cadmium and nickel; and (v) was insensitive to 500 mu M amiloride which abolished the ***T*** - ***type*** at this concentration. The properties of the toxin-resistant current are very similar to those of the currents expressed in oocytes following injection of alpha(1E) subunits which we demonstrated to be present in these neurons. Therefore a component of the toxin-resistant current ***calcium*** ***channels*** in sensory neurons may be closely related to those ***calcium*** ***channels*** formed by alpha(1E) subunits. (C) 1997 IBRO. Published by Elsevier Science Ltd.

L6 ANSWER 83 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:544278 CAPLUS
DOCUMENT NUMBER: 129:258270
TITLE: ***T*** - ***type*** Ca2+ channels expressed during mouse spermatogenesis may mediate sperm acrosome reaction
AUTHOR(S): Darszon, A.; Santi, C. M.; Serrano, C. J.; Trevino, C. L.; Hernandez-Cruz, A.; Lievano, A.
CORPORATE SOURCE: Dep. Genetica Fisiol. Mol., inst. Biotecnologia, Univ. Nacional Autonoma Mexico (UNAM), Cuernavaca, Mex.
SOURCE: Curr. Adv. Androl., Proc. Int. Congr. Androl., 6th (1997), 165-170. Editor(s): Waites, Geoffrey M. H.; Frick, Julian; Baker, Gordon W. H. Monduzzi Editore: Bologna, Italy. CODEN: 66MSAS
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Ion channel are key elements in the mammalian sperm acrosome reaction (AR). Sperm are differentiated terminal cells unable to synthesize protein, and difficult to study electrophysiol. Using mol. biol. to learn about their ion channels requires spermatogenic cells were channel proteins are being synthesized. These cells are larger than sperm and easier to patch clamp. We have looked for the expression of the . ***alpha*** . ***1*** genes, which code for the channel subunit of the various types of voltage-activated Ca2+ channels, in purified spermatogenic cells with RT-PCR. We found that mainly .alpha.1E mRNA is expressed, and increases during spermiogenesis. Interestingly, we only detected ***T*** - ***type*** Ca2+ currents in pachytene spermatocytes. Since these currents are blocked by Ni2+ and dihydropyridines, as is the ZP3 induced AR, it is likely that ***T*** - ***type*** Ca2+ channels play a key role in the Ca2+ uptake required for mammalian sperm AR.

L6 ANSWER 84 OF 104 MEDLINE
ACCESSION NUMBER: 97059901 MEDLINE
DOCUMENT NUMBER: 97059901
TITLE: Structure, function and expression of Ca2+ channels.
AUTHOR: Kameyama A; Kameyama M
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine, Kagoshima University, Japan.
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1996 Mar) 54 (3) 672-8. Ref: 17
Journal code: KIM. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
ENTRY MONTH: 199705
ENTRY WEEK: 19970502
AB Structure, function and expression of voltage-dependent Ca2+ channels are reviewed. Ca2+ channels have been classified into one low-voltage activated subtype (***T*** ***type***) and at least 5 high-voltage activated subtypes (L, N, P, Q and R types), which are characterized by the sensitivity to specific blockers. Although L-type channel in skeletal muscle is shown to consist of ***alpha1*** , alpha2/delta, beta, gamma subunits, it is not clear whether other subtypes have similar subunit structures. Cloning and functional expression of cDNA encoding ***alpha1*** subunits revealed existence of multiple genes and splicing variants. Thus, the diversity in the electrophysiological properties of Ca2+ channels in different tissues and developmental stages comes from, at least in part, the different molecular structure of the channels. Regulation of the expression of Ca2+ channels may be important for the elaborate control of cellular functions.

L6 ANSWER 85 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:940123 CAPLUS
DOCUMENT NUMBER: 124:3114
TITLE: Molecular biology of ***calcium*** ***channels***
AUTHOR(S): Perez-Reyes, Edward; Schneider, Toni
CORPORATE SOURCE: Medical Center, Loyola University, Maywood, IL, USA
SOURCE: Kidney Int. (1995), 48(4), 1111-24
CODEN: KDYIA5; ISSN: 0085-2538
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review, with 156 refs. The mol. biol. of Ca2+ channels has its origins in the biochem. characterization of the skeletal muscle dihydropyridine receptor. These studies established that the dihydropyridine receptor/channel complex was a multi-subunit complex composed of . ***alpha*** . ***1*** (the ion-conducting subunit), and smaller accessory subunits (.alpha.2 .beta., and .gamma.). These subunits were purified, sequenced, cloned, and expressed. Cloning of these cDNAs provided the probes to discover the mol. diversity of Ca2+ channels. To date (Apr. 1995), genes for six .alpha.1s, four .beta.s, one .alpha.2, and one .gamma. have been cloned. Preliminary classification schemes divided native ***calcium*** ***channels*** into low voltage-activated (***T*** - ***type***) and high voltage-activated types: L-type, dihydropyridine-sensitive; and N-type, .omega.-conotoxin GVIA-sensitive. The development of new toxins has led to the further subclassification of high voltage-activated channels to: P-type, which is blocked by .omega.-agatoxin-IVa from the funnel-web spider Agelenopsis aperta; Q-type, which is blocked by .omega.-conotoxin-MVIIC from the marine snail Conus magus; and R-type, which is resistant to most toxins. Expression studies with cloned .alpha.1s have proven that this subunit dets. the voltage and pharmacol. sensitivity of the channel. This should allow the authors' to classify the cloned .alpha.1s in terms of their type. Unfortunately these properties are affected by the choice of expression system, and the subunit compn. of the channel. Despite these complications, the six .alpha.1s have been classified as follows: three .alpha.1s (.alpha.1s, .alpha.1c, and .alpha.1D) belong

to the L-type
(dihydropyridine-sensitive); .alpha.1B is an N-type; .alpha.1A is a P-type
although it has also been classified as Q-type; and .alpha.1E, which does
not display any distinctive pharmacol., has been called an R-type
(resistant). The authors will review the cloning, classification, tissue
distribution, and functional expression of these . ***alpha*** .
1 subunits and the accessory subunits.

L6 ANSWER 86 OF 104 MEDLINE
DUPLICATE 31
ACCESSION NUMBER: 96018848 MEDLINE
DOCUMENT NUMBER: 96018848
TITLE: Voltage-dependent blockade of diverse types of
voltage-gated Ca2+ channels expressed in Xenopus oocytes by
the Ca2+ channel antagonist mibefradil (Ro 40-5967).
AUTHOR: Bezprozvanny I; Tsien R W
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Stanford
University Medical Center, California 94305, USA.
CONTRACT NUMBER: NS24067 (NINDS)
HL07740-02 (NHLBI)
SOURCE: MOLECULAR PHARMACOLOGY., (1995 Sep) 48 (3) 540-9.
Journal code: NGR. ISSN: 0026-895X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199601
AB Four different types of Ca2+ channel ***alpha*** ***1*** subunits,
representing the major classes of voltage-gated Ca2+ channels, were
individually coexpressed along with alpha 2/delta and beta 2b subunits in
Xenopus oocytes. These subunits (and the encoded channel types and major
tissues of origin) included alpha 1C (L-type, cardiac), alpha 1B (N-type,
central nervous system), alpha 1A (P/Q-type, central nervous system), and
alpha 1E (most likely R-type, central nervous system). Divalent cation
currents through these channels (5 mM Ba2+) were evaluated with the
two-microelectrode voltage-clamp technique. The expressed channels were
compared with regard to their responses to a structurally novel,
nondihydropyridine compound, mibefradil (Ro 40-5967). In the micromolar
concentration range, this drug exerted clear inhibitory effects on each of
the four channel types, reducing divalent cation current at all test
potentials, with the non-L-type channels being more sensitive to
inhibition than the L-type channels under fixed experimental conditions.
For all channel types, mibefradil was a much more effective inhibitor at
more depolarized holding potentials, suggesting tighter binding of the
drug to the inactivated state than to the resting state. The difference in
apparent affinities of resting and inactivated states of the channels,
calculated based on a modulated receptor hypothesis, was 30-70-fold. In
addition, the time course of decay of Ca2+ channel current was accelerated
in the presence of drug, consistent with open channel block. The effect of
increasing stimulation frequency was tested for L-type channels and was
found to greatly enhance the degree of inhibition by mibefradil,
consistent with promotion of block by channel opening and inactivation.
Allowing for state-dependent interactions, the drug concentrations found
to block L-, N-, Q-, and R-type channels by 50% are at least 10-fold
higher than half-blocking levels previously reported for ***T*** -
type channels in vascular smooth muscle cells under similar
experimental conditions. This may help explain the ability of the drug to
spare working myocardium (strongly negative resting potential, dominance
of L-type channels in their resting state) while reducing contraction in
blood vessels (presumably involving ***T*** - ***type*** channels or
partially inactivated L-type channels). Thus, mibefradil is a new addition
to the family of nonselective organic Ca2+ channel inhibitors, as
exemplified by bepridil and fluspirilene, and may prove useful as an
experimental tool for studying diverse physiological events initiated by
Ca2+ influx. It complements classes of drugs with relatively selective
effects on L-type channels, as exemplified by nifedipine and diltiazem.

L6 ANSWER 87 OF 104 MEDLINE
DUPLICATE 32
ACCESSION NUMBER: 95378936 MEDLINE
DOCUMENT NUMBER: 95378936
TITLE: Skeletal muscle DHP receptor mutations alter calcium
currents in human hypokalaemic periodic paralysis myotubes
[published erratum appears in J Physiol (Lond) 1998 May
1;508(Pt 3):955].
AUTHOR: Sipos I; Jurkat-Rott K; Harasztosi C; Fontaine B; Kovacs L;
Melzer W; Lehmann-Horn F
CORPORATE SOURCE: Department of Applied Physiology, University of Ulm,
Germany.
SOURCE: JOURNAL OF PHYSIOLOGY, (1995 Mar 1) 483 (Pt 2) 299-306.
Journal code: JQV. ISSN: 0022-3751.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
AB 1. Mutations in the gene encoding the ***alpha*** ***1*** -subunit
of the skeletal muscle dihydropyridine (DHP) receptor are responsible for
familial hypokalaemic periodic paralysis (HypoPP), an autosomal dominant
muscle disease. We investigated myotubes cultured from muscle of patients
with arginine-to-histidine substitutions in putative voltage sensors, IIS4
(R528H) and IVS4 (R1239H), of the DHP receptor ***alpha*** ***1***
-subunit. 2. Analysis of the messenger ribonucleic acid (mRNA) in the
myotubes from such patients indicated transcription from both the normal
and mutant genes. 3. In control myotubes, the existence of the slow L-type
current and of two rapidly activating and inactivating calcium current
components (***T*** - ***type*** with a maximum at about -20 mV and
'third type' with a maximum at +10 to +20 mV) was confirmed. In the
myotubes from patients with either mutation, the third-type current
component was seen more frequently and, on average, with larger amplitude.
4. In myotubes with the IVS4 mutation (R1239H) the maximum L-type current
density was smaller than control (-0.53 +/- 0.31 vs. -1.41 +/- 0.71 pA
pF-1). The voltage dependence of activation was normal, and
hyperpolarizing prepulses to -120 mV for 20 s did not increase the reduced
current amplitude during test pulses. 5. In myotubes with the IIS4
mutation (R528H) the L-type current-voltage relation, determined at a
holding potential of -90 mV, was normal. However, the voltage dependence
of inactivation was shifted by about 40 mV to more negative potentials
(voltage at half-maximum inactivation, V1/2 = -41.5 +/- 8.2 vs. -4.9 +/-
4.3 mV in normal controls).(ABSTRACT TRUNCATED AT 250 WORDS)

L6 ANSWER 88 OF 104 MEDLINE
DUPLICATE 33
ACCESSION NUMBER: 95139756 MEDLINE
DOCUMENT NUMBER: 95139756
TITLE: Tetrandrine: a new ligand to block voltage-dependent Ca2+
and Ca(+)-activated K+ channels.
AUTHOR: Wang G; Lemos J R
CORPORATE SOURCE: Neurobiology Group, Worcester Foundation for Experimental
Biology, Shrewsbury, MA 01545.
CONTRACT NUMBER: NS29470 (NINDS)
SOURCE: LIFE SCIENCES, (1995) 56 (5) 295-306. Ref: 83
Journal code: L62. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199505
AB Extensive pharmacological investigations on tetrandrine, one of the
traditional medicinal alkaloids, are reviewed. Tetrandrine has been used
clinically in China for centuries in the treatment of many diseases. A
recent series of studies has revealed major mechanisms underlying its
multiple pharmacological and therapeutic actions. One of the most
interesting discoveries is that tetrandrine is a new kind blocker of the
voltage-activated, L-type Ca2+ channel in a variety of excitable cells,
such as cardiac, GH3 anterior pituitary and neuroblastoma cells, as well
as in rat neurohypophysial nerve terminals. Although tetrandrine does not
belong to any of the three classical Ca2+ channel blocker groups,
electrophysiological and radioligand binding studies show that tetrandrine
is an L-type Ca2+ channel blocker with its binding site located at the
benzothiazepine receptor on the ***alpha*** ***1*** -subunit of the
channel. In addition, tetrandrine is a blocker of the voltage-dependent
T - ***type*** Ca2+ channel. It is clear that tetrandrine's
actions in the treatment of cardiovascular diseases, including
hypertension and supraventricular arrhythmia, are due primarily to its
blocking of voltage-activated L-type and ***T*** - ***type*** Ca2+
channels. Furthermore, this alkaloid is a potent blocker of the
Ca(2+)-activated K+ (K(Ca)) channels of neurohypophysial nerve terminals.
The blocking kinetics of tetrandrine on the K(Ca) channel is quite
different from that of typical K(Ca) channel blockers such as
tetraethylammonium and Ba2+. Although the clinical role of tetrandrine as
a blocker of the K(Ca) channels is unclear, it is a promising ligand for
the study of K(Ca) channel function.

L6 ANSWER 89 OF 104 MEDLINE
ACCESSION NUMBER: 95406758 MEDLINE

DOCUMENT NUMBER: 95406758
TITLE: Altered calcium currents in human hypokalemic periodic
paralysis myotubes expressing mutant L-type ***calcium*** ***channels*** .
AUTHOR: Lehmann-Horn F; Sipos I; Jurkat-Rott K; Heine R; Brinkmeier H; Fontaine B; Kovacs L; Melzer W
CORPORATE SOURCE: Department of Applied Physiology, University of Ulm, Germany.
SOURCE: SOCIETY OF GENERAL PHYSIOLOGISTS SERIES, (1995) 50 101-13. Journal code: UU2. ISSN: 0094-7733.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199512
AB In a genome-wide search, linkage of hypokalemic periodic paralysis (HypoPP), a muscle disease with autosomal dominant inheritance, to chromosome 1q31-32 and cosegregation with the gene encoding the L-type ***calcium*** ***channel*** /DHP receptor ***alpha*** ***1*** subunit has been reported (Fontaine et al., 1994). Here we show the extended haplotypes of a large HypoPP family who made the detection of the gene product possible. Sequencing of cDNA synthesized from RNA isolated from muscle specimens of two affected family members revealed a G-to-A transition of nucleotide 3716. This base exchange predicts a substitution of histidine for arginine 1239 located in segment IVS4 of the channel protein. By restriction fragment analysis, the mutation was detected in the genomic DNA of all affected family members. Myotubes cultured from the muscle specimens also revealed the mutation suggesting the expression of mutant L-type ***calcium*** ***channel*** /DHP receptors. Whole-cell recordings of 20 such myotubes showed a strong reduction of the DHP sensitive, slowly activating and inactivating L-type current density to 30% of the current in normal controls. A rapidly activating and inactivating current component (third-type), which is distinct from the also occurring ***T*** - ***type*** current, was increased. We conclude that HypoPP is a disease of the skeletal muscle DHP receptor. The point mutation in repeat IV of the protein may have a similar effect as drugs which downregulate the channel activity by binding to this domain.

L6 ANSWER 90 OF 104 MEDLINE
DUPLICATE 34
ACCESSION NUMBER: 95088934 MEDLINE
DOCUMENT NUMBER: 95088934
TITLE: The Ca(++)-channel blocker Ro 40-5967 blocks differently ***T*** - ***type*** and L-type Ca++ channels.
AUTHOR: Mehrke G; Zong X G; Flockerzi V; Hofmann F
CORPORATE SOURCE: Institut fur Pharmakologie und Toxikologie, Technischen Universitat Munchen, Germany.
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1994 Dec) 271 (3) 1483-8. Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
AB The effects of Ro 40-5967, a nondihydropyridine Ca++ channel blocker, on low-voltage activated (***T*** - ***type***) and high-voltage activated (L-type) Ca++ channels were compared. L-type barium currents were measured in Chinese hamster ovary cells stably transfected with the ***alpha*** ***1*** subunit of the class Cb Ca++ channel. ***T*** - ***type*** barium currents were investigated in human medullary thyroid carcinoma cells. The Ba++ currents of human medullary thyroid carcinoma cells were transient, activated at a threshold potential of -50 mV with the maximum at -14 +/- 3.2 mV and blocked by micromolar Ni++. The T- and L-type current inactivated with time constants of 33.4 +/- 4.1 and 416 +/- 26 msec at maximum barium currents, respectively. Ro 40-5967 inhibited reversibly the T- and L-type currents with IC50 values of 2.7 and 18.6 microM, respectively. The inhibition of the L-type current was voltage-dependent, whereas that of the ***T*** - ***type*** current was not. Ro 40-5967 blocked ***T*** - ***type*** current already at a holding potential of -100 mV. The different types of block, i.e., voltage-dependent vs. tonic block, may contribute to the pharmacological profile of Ro 40-5967 in intact animals.

L6 ANSWER 91 OF 104 MEDLINE
DUPLICATE 35
ACCESSION NUMBER: 95088917 MEDLINE
DOCUMENT NUMBER: 95088917
TITLE: Effects of a new class of calcium antagonists, SR33557 (fantofarone) and SR33805, on neuronal voltage-activated Ca++ channels.
AUTHOR: Romey G; Lazdunski M
CORPORATE SOURCE: Institut de Pharmacologie Moleculaire et Cellulaire, Valbonne, France..
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1994 Dec) 271 (3) 1348-52. Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
AB SR33557 (fantofarone) and SR33805 are structurally novel calcium antagonists that bind selectively to the ***alpha*** ***1*** -subunit of the L-type Ca++ channel at a site distinct from the classical 1,4-dihydrophyridine, phenylalkylamine and benzothiazepine sites but in allosteric interactions with them. Blocking effects of fantofarone and SR33805 on the different types of voltage-activated Ca++ currents have been investigated with the whole-cell patch-clamp method in chick dorsal root ganglion neurons (for T-, L- and N-type currents) and in rat cerebellar Purkinje neurons (for P-type current) in primary culture. Neuronal L-type Ca++ channels are blocked totally by fantofarone and SR33805 in the microM range of concentration as in skeletal muscle and cardiac cells at a holding membrane potential of -80 mV. The sequence of efficacy is SR33805 (IC50 = 26 nM) > fantofarone (IC50 = 0.35 microM). N- and P-type channels are not very sensitive to fanto-farone and SR33805 (IC50 approximately 5 microM). The ***T*** - ***type*** channel is not affected by these drugs.

L6 ANSWER 92 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)DUPLICATE 36
ACCESSION NUMBER: 95:50757 SCISEARCH
THE GENUINE ARTICLE: PZ357
TITLE: MOLECULAR DIVERSITY OF ***CALCIUM*** ***CHANNELS*** - FROM GENE TO FUNCTION
AUTHOR: NARGEOT J (Reprint); CHARNET P
CORPORATE SOURCE: CTR RECH BIOCHIM MACROMOLEC, CNRS, UPR 9008, INSERM, U249, BP 5051, ROUTE MENDE, F-34033 MONTPELLIER, FRANCE (Reprint)
COUNTRY OF AUTHOR: FRANCE
SOURCE: M S-MEDECINE SCIENCES, (DEC 1994) Vol. 10, No. 12, pp. 1293-1308. ISSN: 0767-0974.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: French
REFERENCE COUNT: No References Keyed
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Recent studies have revealed the molecular and functional diversity of voltage-gated ***calcium*** ***channels*** . Electrophysiological and pharmacological experiments on various cell types have provided a way of characterizing a Low Voltage Activated (LVA) or " ***T*** - ***type*** ", and several High Voltage Activated (HVA) ***calcium*** ***channels*** . LVA Ca2+ channels have fast kinetics and no specific ligands while HVA Ca2+ channels have been identified mainly by the use of specific toxins, and named L, N, P and Q. They are blocked by dihydropyridines, omega-CgT-GVIA, omega-Aga-IVA and omega-CmT-MVIIC, respectively. Biochemical studies have revealed that skeletal muscle Ca2+ channels are composed of a pore-forming ***alpha*** ***1*** subunit and several associated subunits (alpha 2-delta, beta and gamma). Several ***alpha*** ***1*** subunits have been cloned from various tissues and are encoded by at least six genes. Their expression in Xenopus oocytes or in mammalian cells induces ***calcium*** ***channel*** currents, the properties of which seem to correspond to the different Ca2+ channels identified in various cells. However, it has been suggested that further diversity may be provided by the addition of auxiliary subunits and particularly the beta subunits which are thought to be associated to most of the ***alpha*** ***1*** subunits. beta subunits encoded by at least four genes (beta 1, beta 2, beta 3, beta 4) expressed in the nervous system and other tissues enhance Ca2+ channel activity and are able to modify both electrophysiological and pharmacological properties. However, a differential effect on calcium current inactivation has been observed between the different isoforms (beta 1, beta 2, beta 3) and their splice variants (beta 1a, beta 1b) indicating that multiple Ca2+ channel gating may arise from the expression of different subtypes of beta subunits. The implication of Ca2+ channels in pathophysiology has been recently suggested and the genes coding for ***alpha*** ***1*** or beta subunits are potential candidates in some patho logies. Several autoimmune diseases have also been suggested to involve Ca2+ channels as the targets for antibodies. Moreover, the functional diversity of neuronal Ca2+ channel offers new perspectives in the

development of drugs for the
treatment of neurologic disorders.

L6 ANSWER 93 OF 104 MEDLINE
DUPLICATE 37
ACCESSION NUMBER: 95055196 MEDLINE
DOCUMENT NUMBER: 95055196
TITLE: The L-type ***calcium*** ***channel*** current is
increased by ***alpha*** - ***1*** adrenoceptor
activation in neonatal rat ventricular cells.
AUTHOR: Liu Q Y; Karpinski E; Pang P K
CORPORATE SOURCE: Department of Physiology, University of Alberta, Edmonton,
Canada..
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS,
(1994 Nov) 271 (2) 935-43.
Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199502
AB The activation of ***alpha*** - ***1*** adrenoceptors in adult rat
ventricular cells results in the reduction of the transient outward K+
current, but does not affect Ca++ currents. In this study, using neonatal
rat ventricular cells, the ***alpha*** - ***1*** adrenergic receptor
agonist phenylephrine increased the long-lasting (L-type) Ca++ channel
current (dihydropyridine-sensitive) and the increase was
concentration-dependent. Phenylephrine did not, however, modulate the
transient-type (***T*** - ***type***) Ca++ channel current. The
alpha - ***1*** effect of phenylephrine was reversed or
abolished by prazosin, an ***alpha*** - ***1*** antagonist. The
alpha-2 agonist clonidine had no effect on the L-type current. Yohimbine,
an alpha-2 antagonist, and propranolol, a beta antagonist, did not inhibit
the effect of phenylephrine on L-type current. The effect of phenylephrine
was abolished by pretreatment with WB4101, an alpha-1A antagonist, but not
by chloroethylclonidine, an alpha-1B antagonist. In addition,
norepinephrine also increased the L-type current in the presence of
propranolol and this effect was reversed by washout. These observations
suggest that phenylephrine increased the L-type Ca++ channel current
specifically through the activation of alpha-1A adrenergic receptors in
neonatal rat ventricular myocytes. This may explain in part the increase
in the plateau phase of the action potential and the positive inotropic
response of the neonatal myocardium to phenylephrine. This is the first
description of an increase in L-type Ca++ current by alpha-1A adrenoceptor
activation in neonatal rat ventricular myocytes, and this effect is
different from that reported in adult rat myocytes.

L6 ANSWER 94 OF 104 MEDLINE
DUPLICATE 38
ACCESSION NUMBER: 94354258 MEDLINE
DOCUMENT NUMBER: 94354258
TITLE: ***Calcium*** ***channels*** in excitable cells:
divergent genotypic and phenotypic expression of
alpha ***1*** -subunits.
AUTHOR: Lievano A; Bolden A; Horn R
CORPORATE SOURCE: Roche Institute of Molecular Biology, Nutley, New Jersey
07110.
SOURCE: AMERICAN JOURNAL OF PHYSIOLOGY, (1994 Aug) 267 (2 Pt 1)
C411-24.
Journal code: 3U8. ISSN: 0002-9513.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
AB The Ba2+ currents and mRNA levels of four members of the rat brain family
of ***alpha*** ***1*** -subunit Ca2+ channel genes were examined
and compared in the rat cell lines GH3 and PC-12 and in the mouse lines
NIE-115 and AtT-20. The RNA was measured with ribonuclease protection
assays using probes derived from rat brain (rb) Ca2+ channel cDNAs (rbA,
rbB, rbC, and rbD), and the Ba2+ currents were studied by whole cell
patch-clamp recording. L-, N-, P-, and ***T*** - ***type*** currents
were discriminated by the voltage dependence and pharmacological
properties of Ba2+ currents. All cell lines expressed all four rat brain
Ca2+ channel genes, except GH3 cells, which lacked rbB. The functional
diversity of Ba2+ currents, however, was quite different among the cell
lines. GH3 cells showed evidence of L- and ***T*** - ***type*** currents, undifferentiated PC-12 cells of L-type currents, AtT-20 cells of
L-, N-, and P-type currents, and undifferentiated NIE-115 cells of a
T - ***type*** current that was partially blocked by both
nifedipine and BAY K 8644. Dimethyl sulfoxide-differentiated NIE-115 cells
also had an L-type current. Differentiation of NIE-115 cells caused an
increase in the levels of rbB, rbC, and rbD RNAs. Differentiation by nerve
growth factor caused an increase in levels of all four genes in PC-12. Our
data give further support for the assignment of rbA, rbB, and rbC/rbD gene
products as components of P-, N-, and L-type Ca2+ channels, respectively.

L6 ANSWER 95 OF 104 SCISEARCH
COPYRIGHT 2001 ISI (R)DUPLICATE 39
ACCESSION NUMBER: 95:48824 SCISEARCH
THE GENUINE ARTICLE: QA015
TITLE: TETRANDRINE - A NEW LIGAND TO BLOCK VOLTAGE-DEPENDENT CA2+
AND CA2+-ACTIVATED K+ CHANNELS
AUTHOR: WANG G (Reprint); LEMOS J R
CORPORATE SOURCE: WORCESTER FDN EXPTL BIOL INC, NEUROBIOL GRP, 222 MAPLE AVE, SHREWSBURY, MA, 01545 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: LIFE SCIENCES, (23 DEC 1994) Vol. 56, No. 5, pp. 295-306.
ISSN: 0024-3205.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 81
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Extensive pharmacological investigations on tetrandrine, one of the
traditional medicinal, alkaloids, are reviewed. Tetrandrine has been used
clinically in China for centuries in the treatment of many diseases. A
recent series of studies has revealed major mechanisms underlying its
multiple pharmacological and therapeutic actions. One of the most
interesting discoveries is that tetrandrine is a new kind blocker of the
voltage-activated, L-type Ca2+ channel in a variety of excitable cells,
such as cardiac, GH(3) anterior pituitary and neuroblastoma cells, as well
as in rat neurohypophysial nerve terminals. Although tetrandrine does not
belong to any of the three classical Ca2+ channel blocker groups,
electrophysiological and radioligand binding studies show that tetrandrine
is an L-type Ca2+ channel blocker with its binding site located at the
benzothiazepine receptor on the ***alpha*** (***1***)-subunit of
the channel. In addition, tetrandrine is a blocker of the
voltage-dependent ***T*** - ***type*** Ca2+ channel. It is clear
that tetrandrine's actions in the treatment, of cardiovascular diseases,
including hypertension and supraventricular arrhythmia, are due primarily
to its blocking of voltage-activated L-type and ***T*** - ***type***
Ca2+ channels. Furthermore, this alkaloid is a potent blocker of the
Ca2+-activated K+ (K-(Ca)) channels of neurohypophysial nerve terminals.
The blocking kinetics of tetrandrine on the K-(Ca) channel is quite
different from that of typical K-(Ca) channel blockers such as
tetraethylammonium and Ba2+. Although the clinical role of tetrandrine as
a blocker of the K-(Ca) channels is unclear, it is a promising ligand for
the study of K-(Ca) channel function.

L6 ANSWER 96 OF 104 MEDLINE
DUPLICATE 40
ACCESSION NUMBER: 95121362 MEDLINE
DOCUMENT NUMBER: 95121362
TITLE: Effects of two chemically related new Ca2+ channel
antagonists, SR33557 (fantofarone) and SR33805, on the
L-type cardiac channel.
AUTHOR: Romey G; Bois P; Lazdunski M
CORPORATE SOURCE: Institut de Pharmacologie Moleculaire et Cellulaire, Sophia
Antipolis, Valbonne, France..
SOURCE: EUROPEAN JOURNAL OF PHARMACOLOGY, (1994 Sep 22) 263 (1-2)
101-5.
Journal code: EN6. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504
AB Fantofarone (SR33557) is a substituted indolizine and SR33805 is a
substituted indole. These drugs have been shown to specifically bind to
the ***alpha*** ***1*** subunit of the L-type Ca2+ channel at the
same site, distinct from those of the classical 1,4-dihydropyridine,
phenylalkylamine or benzothiazepine Ca2+ antagonists, but in negative
allosteric interaction with them. The present work shows that fantofarone
and SR33805 block L-type but not ***T*** - ***type*** Ca2+ channels
in mouse cardiac cells in primary culture. This block is
voltage-dependent. Fantofarone and SR33805 are potent Ca2+ channel
blockers in depolarized conditions (i.e. at a holding potential of -40 mV)
with an EC50 = 1.4 and 4.1 nM, respectively. In polarized conditions (i.e.
at a holding potential of -80 mV), SR33805 is a better Ca2+ channel
blocker (EC50 = 33 nM) than fantofarone (EC50 = 0.15 microM). Therefore
differences in their chemical structures make the blocking action of
fantofarone more sensitive to voltage than that of SR33805.

L6 ANSWER 97 OF 104 MEDLINE

ACCESSION NUMBER: 93308850 MEDLINE
DOCUMENT NUMBER: 93308850
TITLE: Molecular structure and functional sites of the cardiac
calcium ***channels*** .
AUTHOR: Nakayama H
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Hokkaido University..
SOURCE: NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1993 Jun) 51 (6) 1471-6. Ref: 16
Journal code: KIM. ISSN: 0047-1852.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: Japanese
ENTRY MONTH: 199310
AB Voltage gated L-type and ***T*** - ***type*** ***calcium***
channels are electrophysiologically characterized in the cardiac
tissues. L-Type ***calcium*** ***channels*** are abundant in
skeletal muscle and results from molecular studies have stimulated
researches on the cardiac counterpart. This paper briefly reviews the
recent progress in molecular constituents and functional sites of the
cardiac ***calcium*** ***channel*** . The channel is composed of
five subunits, ***alpha*** ***1*** , alpha 2, beta, gamma, and
delta, at least, but heterogeneous existence of ***alpha*** ***1***
, beta, and gamma is also observed. The 1,4-dihydropyridine binding site
has been identified in the skeletal muscle and cardiac ***calcium***
channels by photoaffinity labeling. Their sites are compared in
the primary structures. PKA modulation of the cardiac channel is also
discussed with the respect to phosphorylation site.

L6 ANSWER 98 OF 104 MEDLINE
DUPLICATE 41
ACCESSION NUMBER: 94150810 MEDLINE
DOCUMENT NUMBER: 94150810
TITLE: Distinctive pharmacology and kinetics of cloned neuronal
Ca2+ channels and their possible counterparts in mammalian
CNS neurons.
AUTHOR: Zhang J F; Randall A D; Ellinor P T; Horne W A; Sather W A;
Tanabe T; Schwarz T L; Tsien R W
CORPORATE SOURCE: Department of Molecular and Cellular Physiology, Stanford
University Medical Center, CA 94305.
CONTRACT NUMBER: GM42376 (NIGMS)
NS24067 (NINDS)
SOURCE: NEUROPHARMACOLOGY, (1993 Nov) 32 (11) 1075-88. Ref: 40
Journal code: NZB. ISSN: 0028-3908.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199405
AB This paper provides a brief overview of the diversity of voltage-gated
Ca2+ channels and our recent work on neuronal Ca2+ channels with novel
pharmacological and biophysical properties that distinguish them from L,
N, P or ***T*** - ***type*** channels. The Ca2+ channel
alpha ***1*** subunit known as alpha 1A or BI [Mori Y.,
Friedrich T., Kim M.-S., Mikami A., Nakai J., Ruth P., Bosse E., Hofmann
F., Flockerzi V., Furuichi T., Mikoshiba K., Imoto K., Tanabe T. and Numa
S. (1991) Nature 350, 398-402] is generally assumed to encode the P-type
Ca2+ channel. However, we find that alpha 1A expressed in Xenopus oocytes
differs from P-type channels in its kinetics of inactivation and its
degree of sensitivity to block by the peptide toxins omega-Aga-IVA and
omega-CTx-MVIIC [Sather W. A., Tanabe T., Zhang J.-F., Mori Y., Adams M.
E. and Tsien R. W. (1993) Neuron 11, 291-303]. Thus, alpha 1A is capable
of generating a Ca2+ channel with characteristics quite distinct from
P-type channels. Doe-1, recently cloned from the forebrain of a marine
ray, is another ***alpha*** ***1*** subunit which exemplifies a
different branch of the Ca2+ channel family tree [Horne W. A., Ellinor P.
T., Inman I., Zhou M., Tsien R. W. and Schwarz T. L. (1993) Proc. Natn.
Acad. Sci. U.S.A. 90, 3787-3791]. When expressed in Xenopus oocytes, doe-1
forms a high voltage-activated (HVA) Ca2+ channel [Ellinor P. T., Zhang
J.-F., Randall A. D., Zhou M., Schwarz T. L., Tsien R. W. and Horne W.
(1993) Nature 363, 455-458]. It inactivates more rapidly than any
previously expressed ***calcium*** ***channel*** and is not
blocked by dihydropyridine antagonists or omega-Aga-IVA. Doe-1 current is
reduced by omega-CTx-GVIA, but the inhibition is readily reversible and
requires micromolar toxin, in contrast to this toxin's potent and
irreversible block of N-type channels. Doe-1 shows considerable
sensitivity to block by Ni2+ or Cd2+. We have identified components of
Ca2+ channel current in rat cerebellar granule neurons with kinetic and
pharmacological features similar to alpha 1A and doe-1 in oocytes [Randall
A. D., Wendland B., Schweizer F., Miljanich G., Adams M. E. and Tsien R.
W. (1993) Soc. Neurosci. Abstr. 19, 1478]. The doe-1-like component
(R-type current) inactivates much more quickly than L, N or P-type
channels, and also differs significantly in its pharmacology.(ABSTRACT
TRUNCATED AT 400 WORDS)

L6 ANSWER 99 OF 104 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:431912 CAPLUS
DOCUMENT NUMBER: 121:31912
TITLE: Retinol stimulates amino acid transport in Sertoli
cell by a Ca2+ related mechanism
AUTHOR(S): Wassermann, G. F.; Silva, F. R. M. B.; Grillo, M. L.;
Loss, E. S.; Leite, L.; von Ledebur, E. I. C. F.
CORPORATE SOURCE: Inst. de Biocienc., Univ. Fed. do Rio Grande do Sul,
Porto Alegre, Brazil
SOURCE: Med. Sci. Res. (1993), 21(11), 437-8
CODEN: MSCREJ; ISSN: 0269-8951
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Retinol stimulated the transport of . ***alpha*** .-[***1***
-14C]-methylaminoisobutyric acid by Sertoli cells in culture or in Sertoli
cell-enriched testis of immature rat. This effect was mediated by
voltage-dependent Ca2+ channels, probably of the ***T*** - ***type***
.

L6 ANSWER 100 OF 104 MEDLINE
ACCESSION NUMBER: 94033707 MEDLINE
DOCUMENT NUMBER: 94033707
TITLE: Crooked neck dwarf (cn) mutant chicken skeletal muscle
cells in low density primary cultures fail to express
normal alpha ryanodine receptor and exhibit a partial
mutant phenotype.
AUTHOR: Airey J A; Deerinck T J; Ellisman M H; Houenou L J;
Ivanenko A; Kenyon J L; McKemy D D; Sutko J L
CORPORATE SOURCE: Department of Pharmacology, University of Nevada School of Medicine, Reno 89557.
CONTRACT NUMBER: RR04050 (NCRR)
SOURCE: DEVELOPMENTAL DYNAMICS, (1993 Jul) 197 (3) 189-202.
Journal code: A9U. ISSN: 1058-8388.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
AB The Crooked Neck Dwarf (cn) mutation in chickens causes marked changes in
intact embryonic skeletal muscle. We have investigated whether the cn/cn
phenotype develops in vitro, and if cultured muscle cells are suitable for
studies of this mutation. The properties of cn/cn muscle cells maintained
in low density primary cultures (6.25 x 10(3) cells/cm2) are described in
this report. In normal muscle cells, the alpha ryanodine receptor (RyR)
isoform appears prior to, and at greater levels than, the beta RyR, and is
detected in mononucleated myocytes. The beta RyR isoform appears within 24
hr after the initiation of myotube formation, which is earlier than
anticipated from studies with intact embryonic muscle. Normal alpha RyR
protein is not detected in cultured cn/cn muscle cells, whereas the beta
RyR, the ***alpha*** ***1*** -subunit of the dihydropyridine
receptor, the sarcoplasmic reticulum Ca(2+)-ATPase, and calsequestrin are
expressed at comparable levels in normal and mutant muscle cells. Calcium
transients elicited by electrical stimulation, acetylcholine, and caffeine
are similar in normal and cn/cn cultured myotubes and are blocked by
ryanodine in both cell types. In addition, comparable L- and ***T*** -
type calcium currents are observed in normal and mutant muscle
cells, suggesting that both the ***alpha*** ***1*** -subunit of the
dihydropyridine receptor and the beta RyR in mutant muscle cells are
functional. Normal and cn/cn muscle cells proliferate and form myotubes in
a similar manner. These latter events do not appear to depend on
sarcoplasmic reticulum calcium release, as they also occur in normal
muscle cells in which calcium release is prevented by chronic treatment
with 100 microM ryanodine. Both cn/cn and ryanodine-treated normal muscle
cells exhibit morphological changes similar to those observed in intact
cn/cn skeletal muscle. Thus, the mutant phenotype observed in ovo is
partially expressed under low density culture conditions, and neither beta
RyR protein nor its function appear to be capable of preventing the
associated changes.

L6 ANSWER 101 OF 104 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 92:559744 SCISEARCH
THE GENUINE ARTICLE: JN810
TITLE: PROPERTIES OF THE LOW THRESHOLD CA CURRENT IN SINGLE FROG ATRIAL CARDIOMYOCYTES - A COMPARISON WITH THE HIGH THRESHOLD CA CURRENT

AUTHOR: ALVAREZ J L; VASSORT G (Reprint)
CORPORATE SOURCE: UNIV PARIS 11, UNITE RECH PHYSIOL CELLULAIRE CARDIAQ, INSERM, U241, BAT 443, F-91405 ORSAY, FRANCE; INST CARDIOL & CIRUG CARDIOVASC, ELECTROFISIOL LAB, HAVANA 10600, CUBA
COUNTRY OF AUTHOR: FRANCE; CUBA
SOURCE: JOURNAL OF GENERAL PHYSIOLOGY, (SEP 1992) Vol. 100, No. 3, pp. 519-545.
ISSN: 0022-1295.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 68
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB The properties of the low threshold Ca current (I(CaT)) in bullfrog (Rana catesbeiana) isolated atrial cardiomyocytes were studied using the whole-cell recording patch-clamp technique and compared with those of the high threshold Ca current (I(CaL)). In 91% of atrial cells we observed both I(CaT) and I(CaL) when collagenase and trypsin were used to dissociate the cells. But when pronase was used, only 30% of the cells exhibited I(CaT). I(CaT) was never found in ventricular cells. I(CaT) could be investigated more easily when I(CaL) was inhibited by Cd ions (50-mu-M). Its kinetics were unchanged by substituting Ba for Ca, or in the presence of high concentrations of Ba. Both I(CaT) and I(CaL) exhibited reduced inactivation after high depolarizing prepulses. I(CaT) was found to be sensitive to dihydropyridines: 1-mu-M nifedipine decreased this current while 1-mu-M BAY K 8644 increased it; this occurred without significant variations in the steady-state inactivation curve. I(CaT) was more sensitive than I(CaL) to ***alpha*** - ***1*** -adrenergic and P2-purinergic stimulations, while I(CaL) Was more sensitive to beta-adrenergic stimulation. Isoproterenol was still able to increase I(CaT) in the presence of high intracellular cAMP. Both currents were increased by 1-mu-M ouabain (although I(CaL) only transiently) and decreased by 10-mu-M ouabain. It is concluded that the two types of Ca channels can be observed in bullfrog atrial cells and that they are specifically altered by pharmacological agents and neuromediators. This may have implications for cardiac behavior.

L6 ANSWER 102 OF 104 MEDLINE
DUPLICATE 42
ACCESSION NUMBER: 89130135 MEDLINE
DOCUMENT NUMBER: 89130135
TITLE: Modulation of ***calcium*** ***channels*** in cardiac and neuronal cells by an endogenous peptide.
AUTHOR: Callewaert G; Hanbauer I; Morad M
CORPORATE SOURCE: Department of Physiology, School of Medicine, University of Pennsylvania, Philadelphia 19104.
CONTRACT NUMBER: HL16152 (NHLBI)
SOURCE: SCIENCE, (1989 Feb 3) 243 (4891) 663-6.
Journal code: UJ7. ISSN: 0036-8075.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198905
AB ***Calcium*** ***channels*** mediate the generation of action potentials, pacemaking, excitation-contraction coupling, and secretion and signal integration in muscle, secretory, and neuronal cells. The physiological regulation of the L-type ***calcium*** ***channel*** is thought to be mediated primarily by guanine nucleotide-binding proteins (G proteins). A low molecular weight endogenous peptide has been isolated and purified from rat brain. This peptide regulates up and down the cardiac and neuronal ***calcium*** ***channels*** , respectively. In cardiac myocytes, the peptide-induced enhancement of the L-type calcium current had a slow onset (half-time approximately 75 seconds), occurred via a G protein-independent mechanism, and could not be inhibited by ***alpha*** ***1*** -adrenergic, beta-adrenergic, or angiotensin II blockers. In neuronal cells, on the other hand, the negative effect had a rapid onset (half-time less than 500 milliseconds) and was observed on both ***T*** - ***type*** and L-type ***calcium*** ***channels*** .

L6 ANSWER 103 OF 104 MEDLINE
ACCESSION NUMBER: 89301359 MEDLINE
DOCUMENT NUMBER: 89301359
TITLE: ***Calcium*** ***channels*** reconstituted from the skeletal muscle dihydropyridine receptor protein complex and its ***alpha*** ***1*** peptide subunit in lipid bilayers.
AUTHOR: Pelzer D; Grant A O; Cavalie A; Pelzer S; Sieber M; Hofmann F; Trautwein W
CORPORATE SOURCE: II. Physiologisches Institut, Medizinische Fakultat, Universitat des Saarlandes, Homburg/Saar, Federal Republic of Germany.
SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1989) 560 138-54.
Journal code: 5NM. ISSN: 0077-8923.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 198910
AB In the first part of this study, we show that sDHPR and pDHPR preparations reconstituted into lipid bilayers formed on the tips of patch pipettes exhibit two divalent cation-selective conductance levels of 9 and 20 pS, similar in single-channel conductance to VSCC reported in a variety of intact preparations (see Pelzer et al. and Tsien et al. for review). The larger conductance level is similar to the VSCC identified in intact rat t-tubule membranes and described in sDHPR and pDHPR preparations, and shares many properties in common with activity from L-type VSCC. It is sensitive to augmentation by the DHP agonist (+/-)-BAY K 8644 and cAMP-dependent phosphorylation, and to block by the phenylalkylamine (+/-)-D600 and the inorganic blocker CoCl2. Its open-state probability and open times are increased upon depolarization as expected for a voltage-dependent activation process. Upon depolarization beyond the reversal potential, however, open-state probability and open times decline again. A reasonable way to explain the bell-shaped dependence of open times and open-state probability on membrane potential is to assume voltage-dependent ion-pore interactions that produce closing of the channel at strong negative and positive membrane potentials. By contrast, the smaller conductance level may be similar to the 10.6-pS t-tubule VSCC described by Rosenberg et al. and may best be compared with ***T*** - ***type*** VSCC. It is largely resistant to augmentation by (+/-)-BAY K 8644 and cAMP-dependent phosphorylation or block by (+/-)-D600, but is sensitive to block by CoCl2. Its open times and open-state probability show a sole dependence on membrane potential where depolarization increases both parameters sigmoidally from close to zero up to a saturating level. Both elementary conductance levels do not exhibit significant inactivation over a wide potential range, which may suggest that skeletal muscle VSCC inactivation is either poorly or not voltage-dependent at all. This possibility seems in agreement with bilayer recordings on reconstituted intact t-tubule membranes and voltage-clamp recordings on intact fibers. It supports the idea that the decline of Ca2+ current in intact skeletal muscle fibers may be due to Ca2+ depletion from the t-tubule system and/or to inactivation induced by Ca2+ release from the sarcoplasmic reticulum. We consistently observe two conductance levels of 9 and 20 pS, either singly, or together in the same bilayer from solubilized DHPR samples and even highly purified DHPR preparations.(ABSTRACT TRUNCATED AT 400 WORDS)

L6 ANSWER 104 OF 104 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 88139593 EMBASE
DOCUMENT NUMBER: 1988139593
TITLE: Structure and pharmacology of voltage-dependent ***calcium*** ***channels*** .
AUTHOR: Glossmann H.; Striessnig J.
CORPORATE SOURCE: Institute of Biochemical Pharmacology, University of Innsbruck, A-6020 Innsbruck, Austria
SOURCE: ISI Atlas of Science: Pharmacology, (1988) 2/2 (202-210).
ISSN: 0890-9083 CODEN: IASPEP
COUNTRY: United States
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Voltage-dependent Ca2+ channels are classified into L-, N-, and ***T*** - ***types*** . The L-type is sensitive to organic drugs (1,4-dihydropyridines, phenylalkylamines, benzothiazepines, diphenylbutylpiperidenes, etc.) and the N-type (occurring on neurons) is blocked by the peptide toxin .omega.-conotoxin GVIA, whereas the ***T*** - ***type*** (occurring on neurons and, for example, heart cells) is not modulated by 1,4-dihydropyridines but is inhibited by gallopamil, cinnarizine, and amiodarone. Purification, reconstitution, and molecular cloning of an essential (drug receptor-carrying) constituent, the . ***alpha*** . ***1*** sub-unit, have been achieved with 'L-type' Ca2+ channels from skeletal muscle transverse-tubule membranes. The . ***alpha*** . ***1*** subunit is believed to play a role in excitation-contraction coupling in skeletal muscle. L-type Ca2+ channel

activity in situ is regulated by hormone and neurotransmitter receptors
indirectly via second messengers (cyclic adenosine monophosphate) and
perhaps more directly via guanyl nucleotide signal transduction proteins.
L-type Ca2+ channel . ***alpha*** . ***1*** polypeptides similar in
size to those in skeletal muscle have been identified in brain and heart
membranes, but information on their primary structure is not yet
available. Structural characterization of N-type channels is just
beginning, and no structural information is yet available about ***T***
- ***type*** Ca2+ channels.

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